
From: Berkson, Laura (NIH/OD) [E] [/O=NIH/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=DAMIANOLD]
Sent: 7/7/2017 9:08:23 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=OD/cn=ROHRBAUM]; Culhane, Ned (NIH/OD) [E] [/O=NIH/OU=Nihexchange/cn=recipients/cn=culhanee]
Subject: RE: DoD bill language

The links I sent earlier were to the House bill. The Senate bill was marked up in a closed setting and I don't think the text is public yet. <https://www.armed-services.senate.gov/hearings/115-06-28-schedule-for-armed-services-full-committee-markup-of-the-national-defense-authorization-act-for-fiscal-year-2018>

From: Berkson, Laura (NIH/OD) [E]
Sent: Friday, July 07, 2017 4:42 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>; Culhane, Ned (NIH/OD) [E] <culhanee@mail.nih.gov>
Subject: RE: DoD bill language

Here's another article on the amendment: <https://www.statnews.com/pharma/2017/07/06/xtandi-zika-king-amendment-defense/>. Note that the link for the amendment is to Sen. King's press release, not the actual text.

A proposal would limit prices on meds developed with Defense Department dollars

By [ED SILVERMAN](#) @PharmaLot
JULY 6, 2017
AFP / GETTY IMAGES

U.S. senator is trying to lower prices for medicines that are discovered with taxpayer dollars, and his effort amounts to a new twist to unraveling a complicated controversy that has embroiled the U.S. Department of Defense, large drug makers, numerous lawmakers, and consumer groups. Late last month, Angus King (I-Maine) successfully added an [amendment](#) to a Defense Department funding bill that consumer groups say would effectively allow an end run around drug makers that priced products — which were developed with taxpayer dollars — higher than what is charged in seven other countries. The trigger would be determined by median prices and per capita income compared with the U.S.

The move comes amid heightened debate over the extent to which companies should be permitted to profit from medical inventions that are funded — at least, in part — with U.S. taxpayer dollars.

[One example](#) is the Xtandi prostate cancer drug, which was originally invented at the University of California, Los Angeles, with grants from the National Institutes of Health and the Department of Defense. One of the chief inventors was a professor at UCLA, which then licensed the drug to

Medivation. That company then struck a marketing deal with Astellas, and Medivation was later acquired by Pfizer.

The drug has an average wholesale price in the U.S. of more than \$129,000, about two to four times more than what other high-income countries are paying, according to the Union for Affordable Cancer Treatment and Knowledge Ecology International. The groups have pointed out that Medicare paid more than \$790 million in 2015, up from \$447 million in 2014, and the pricing led to high co-payments.

Meanwhile, the U.S. Army may offer an exclusive license for a Zika virus vaccine to Sanofi. A growing number of lawmakers are concerned that a vaccine would not be accessible or affordable for many Americans, since the company would have monopoly rights through 2036. Lawmakers want the Army to offer a non-exclusive license after Sanofi ~~rejected~~ an Army request to offer a pricing commitment.

Some lawmakers and consumer groups have tried various tactics to win assurances for taxpayers that these products will be accessible, but have so far met with little success. The amendment offered by King, which a spokeswoman explained will not become available until next week, appears to be the first such effort to tie Defense Department funding to prices of medicines that were developed with taxpayer dollars.

In a statement issued late last month, King's office said "the provision directs the Department of Defense to authorize third parties to use inventions that benefited from department funding whenever the price of a drug, vaccine, or other medical technology is higher in the U.S. than the median price charged in the seven largest economies that have a per capita income at least half the per capita income of the U.S."

"Senator King's amendment would protect U.S. residents from paying more than everyone else for drugs based upon inventions when the Department of Defense funded the R&D," said Jamie Love of KEI. "To put it in very non-technical terms, the bottom line is the government would break a monopoly if a company was screwing Americans."

Love believes the amendment would allow the federal government to issue so-called march-in rights, which refer to overriding a patent. Under federal law, this allows an agency that funds private research to require a drug maker to license its patent to another party in order to "alleviate health and safety needs which are not being reasonably satisfied" or when the benefits of a drug are not available on "reasonable terms."

Consumer groups have asked the Trump administration to ~~pursue this approach~~ for Xtandi, but have so far not received a reply. The same request was made to the Obama administration, but the National Institutes of Health, which the groups had petitioned, rejected the request.

A spokeswoman for the Pharmaceutical Research & Manufacturers of America, the industry trade group, wrote us that the amendment "ignores the subsequent substantial R&D investments and risks undertaken by the private sector in developing and bringing a new medicine to patients. This amendment would undermine critical intellectual property rights and incentives, create substantial uncertainty for companies, and establish completely arbitrary criteria for taking intellectual property.

This could chill critically needed collaborations and investment by the private sector to address some of our most serious unmet medical needs.”

Spokespeople for Astellas and Pfizer declined comment. We asked Sanofi for comment and will update you accordingly.

Meanwhile, several congressional lawmakers recently wrote to Sanofi, saying they would urge the Army not to finalize any contracts with the drug makers unless a deal was reached to provide a reasonable and affordable price for a finished Zika vaccine. Other lawmakers have asked the Army to hold a hearing on its licensing process and negotiations with Sanofi, but the Army has not indicated if it will do so.

A Sanofi executive recently indicated a price has not been set, but the company intends to price any vaccine in order to “facilitate access” in the interest of public health and is not pursuing the project for a “commercial return.” Another executive previously indicated that royalties would be paid, but details have not been released as negotiations continue.

Contact the Author

Ed Silverman can be reached at ed.silverman@statnews.com

Follow Ed on Twitter @Pharmalot

From: Berkson, Laura (NIH/OD) [E]
Sent: Friday, July 07, 2017 2:29 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>; Culhane, Ned (NIH/OD) [E] <culhanee@mail.nih.gov>
Subject: RE: DoD bill language

Thanks, Mark. I don't see the language in the NDAA bill that was ordered to be reported by the Armed Services Committee last week. I'll keep looking through the amendments that were offered and let you know if I find it.

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Friday, July 07, 2017 2:17 PM
To: Culhane, Ned (NIH/OD) [E] <culhanee@mail.nih.gov>; Berkson, Laura (NIH/OD) [E] <laura.berkson@nih.gov>
Subject: DoD bill language

Someone on the outside told me this is the language:

“The Department of Defense shall exercise the rights under 35 USC 209(d)(1) or 35 USC 203 to authorize third parties to use inventions that benefited from Department of Defense funding whenever the price of a drug, vaccine or other medical technology is higher in the United States than the median price charged in the seven largest economies that have a per capita income at least half the per capita income of the United States.”

Mark L. Rohrbaugh, Ph.D., J.D.
Special Advisor for Technology Transfer
Director, Division of Technology Transfer and Innovation Policy
Office of Science Policy
Office of the Director

From: Dodson, Sara (NIH/NIAID) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=985A956EAA0D4945BDCFD8EA30947D68-DODSONSE]
Sent: 7/24/2018 3:35:43 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718ccb29fab-rohrbaum]
Subject: RE: CONFIDENTIAL list of attendees for Harvard meeting

Hi Mark -

b6

b6

-----Original Message-----

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Thursday, July 19, 2018 5:39 PM
To: Dodson, Sara (NIH/NIAID) [E] <sara.dodson@nih.gov>; Gadbois, Ellen (NIH/OD) [E] <gadboisel@od.nih.gov>
Subject: CONFIDENTIAL list of attendees for Harvard meeting

I was invited to this closed meeting in Dec about " of government funding of drug development and the different strategies that are currently taken (and that have been proposed) to account for that contribution"

b5 has been active writing for years about use of march-in to reduce prices. b6
you probably know. We know b6
b6 are in the same camp. Of course we know b6 (odd that he would be coming). Do you know any of the others and their general positions on issues like this?

-----Original Message-----

From: Kesselheim, Aaron Seth,M.D.,M.P.H. <akesselheim@bwh.harvard.edu>
Sent: Thursday, July 19, 2018 5:30 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Subject: RE: Questions about CRADAs

We hope so. The (at this point, confidential) list of other invitees is below. We would welcome your participation as a member of the conversation throughout the meeting, or for a half-day period, or even as a guest speaker at lunch or dinner. We will operate under 'Chatham House Rules' such that there will be no quotes attributed to anyone.

Let me know what you think! We believe it will be very useful to have your perspective and contribution-

Best,
Aaron

b6

-----Original Message-----

From: Rohrbaugh, Mark (NIH/OD) [E] [mailto:rohrbaum@od.nih.gov]
Sent: Thursday, July 19, 2018 5:05 PM
To: Kesselheim, Aaron Seth,M.D.,M.P.H. <akesselheim@bwh.harvard.edu>
Subject: RE: Questions about CRADAs

External Email - Use Caution

Aaron:

REL0000024391

I am considering your invitation to the Dec meeting. Will the attendees represent a breadth of thinking and opinions about this issue?

Thanks
Mark

-----Original Message-----

From: Kesselheim, Aaron Seth,M.D.,M.P.H. <akesselheim@bwh.harvard.edu>
Sent: Wednesday, July 18, 2018 4:05 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Subject: RE: Questions about CRADAs

So noted! This is all for our background knowledge. Thanks for responding!

Any initial thoughts about joining us in Boston for the December event?

ASK

-----Original Message-----

From: Rohrbaugh, Mark (NIH/OD) [E] [mailto:rohrbaum@od.nih.gov]
Sent: Wednesday, July 18, 2018 4:03 PM
To: Kesselheim, Aaron Seth,M.D.,M.P.H. <akesselheim@bwh.harvard.edu>
Subject: RE: Questions about CRADAs

External Email - Use Caution

Aaron:

Note that I do not give permission to publish or otherwise publicize my direct comments without permission.

By the late 1980s, NIH was using one standard model agreement for all types of CRADA collaborations. We noted later that some types of collaborations required fewer terms in this standard agreement. In particular, when the collaboration involved primarily the receipt and training in the use of unique research materials from a company, terms dealing with other matters such as human subjects, reports from the company, regular meetings between the parties, etc. were not relevant and therefore not needed. Rather than send a company lawyer a document with a number of nonrelevant terms to be deleted, NIH developed a M-CRADA stripped down to the terms relevant to or otherwise legally required in a collaboration involving primarily materials. It sped up negotiation and thus benefited both the NIH and the company providing the unique materials.

Since then other CRADA models were developed to suit particular types of commercial collaborations, e.g. clinical research.

CRADA partners do not decide on which model, NIH decides.

-----Original Message-----

From: Kesselheim, Aaron Seth,M.D.,M.P.H. <akesselheim@bwh.harvard.edu>
Sent: Wednesday, July 18, 2018 11:21 AM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Subject: RE: Questions about CRADAs

Thanks Mark! This is very useful--I will read this over. Here are the questions we have, which may not be covered by this overview:

1. What's the difference between a CRADA and a Materials CRADA (MCRADA)? In particular, are there any cost benefits or differences in accessibility between a CRADA and an MCRADA?
2. Prior to 1996 (when the NIH initiated MCRADAs), could any of the signed CRADAs cover what is now included in an MCRADA?
3. How do potential CRADA partners decide between a CRADA and a MCRADA?
4. What motivated the NIH to introduce the MCRADA mechanism in 1996?

Let me know if this is worth a phone call.

On a different note, we're organizing a Radcliffe Seminar at Harvard this winter (December 11-12) on the subject of government funding of drug development and the different strategies that are currently taken (and that have been proposed) to account for that contribution. It's a small group session of like 15 or so experts in science, economics, law, and medicine from around the country. It would be great to have you join us if not for the whole time, at least as a guest/featured speaker over lunch or dinner -- would something like that be possible?

Best,
Aaron

-----Original Message-----

From: Rohrbaugh, Mark (NIH/OD) [E] [mailto:rohrbaum@od.nih.gov]
Sent: Wednesday, July 18, 2018 11:16 AM

To: Kesselheim, Aaron Seth,M.D.,M.P.H. <akesselheim@bwh.harvard.edu>
Subject: RE: Questions about CRADAs

External Email - Use Caution

Here is NIH's overview of CRADAs. <https://www.ott.nih.gov/policy/cradas>

-----Original Message-----

From: Kesselheim, Aaron Seth,M.D.,M.P.H. <akesselheim@bwh.harvard.edu>
Sent: Tuesday, July 17, 2018 10:43 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Subject: Questions about CRADAs

Hi Mark -- hope all is well. One of the people in my research group is doing a project on CRADAs and had a few fundamental questions that I thought you might be able to help with -- would it be ok to send the questions over email, or maybe set up a time to quickly chat?

Best,
Aaron

Aaron S. Kesselheim, M.D., J.D., M.P.H.
Associate Professor of Medicine at Harvard Medical School Director, Program On Regulation, Therapeutics, And Law (PORTAL) Division of Pharmacoepidemiology and Pharmacoconomics Brigham and Women's Hospital
1620 Tremont St, Suite 3030
Boston MA 02120
akesselheim@partners.org
P: 617-278-0930; F: 617-232-8602
<http://www.PORTALresearch.org>

Faculty member, Harvard Medical School Center for Bioethics Irving S. Ribicoff Visiting Associate Professor of Law, Yale Law School (2016-2018) Editor-in-Chief, Journal of Law, Medicine, and Ethics

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REL0000024391

From: Fine, Amanda (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=61290B74AA9A44358954C45439FFDEB6-FINEAB]
Sent: 10/17/2017 2:43:40 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
CC: Myles, Renate (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=7d317f5626934585b3692a1823c1b522-mylesr]; Wojtowicz, Emma (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=45c6610aca6e44a08d497630425e5ecd-wojtowiczem]
Subject: FW: question from a journalist
Attachments: HHS, Penn CAR Tpatent disclosures 17Oct2017, final.pdf

Hi Mark-

ASPA forwarded the below inquiry from Ed Silverman about the attached KEI letter to the Secretary about patents to CAR T technologies used by UPenn researchers. KEI's letter asks for an investigation because it claims that these PIs didn't mention NIH/federal funding or that the technologies included NIH patented inventions.

b5

Please let me know if you need any additional information.

Thanks!
Amanda

From: OS Media (HHS/ASPA) [mailto:media@hhs.gov]
Sent: Tuesday, October 17, 2017 10:04 AM
To: Fine, Amanda (NIH/OD) [E] <amanda.fine@nih.gov>; Wojtowicz, Emma (NIH/OD) [E] <emma.wojtowicz@nih.gov>
Cc: OS Media (HHS/ASPA) <media@hhs.gov>
Subject: FW: question from a journalist

From: Silverman, Ed [<mailto:ed.silverman@statnews.com>]
Sent: Tuesday, October 17, 2017 9:56 AM
To: OS Media (HHS/ASPA)
Subject: question from a journalist

Hi

My name is Ed Silverman and I run the Pharmalot blog at The Boston Globe's STAT health and medicine site.

An advocacy group called Knowledge Ecology International wrote the HHS yesterday, alleging that the University of Pennsylvania failed to disclose that five patents for a particular cancer treatment called CAR-T were developed with federal funds provided by NIH.

The group wrote to Acting Secretary Hargan that "the Bayh-Dole Act requires that companies disclose when public funds are used to create an invention. These disclosures should be made on the application for the patent and printed on the patent in a "Statement Regarding Federally Sponsored Research Or Development."

Their letter is attached.

The HHS was asked to investigate and I would like to know if an investigation will be undertaken to determine whether the disclosure was made appropriately or not.

Thanks,
Ed Silverman
973-493-7851
www.statnews.com/pharmalot/



1621 Connecticut Ave NW Suite 500
Washington, D.C. 20009
+1 (202) 332-2670
<http://keionline.org>

October 16, 2017

The Honorable Eric D. Hargan
Acting Secretary
Department of Health and Human Services
200 Independence Avenue, S.W.
Washington, D.C. 20201
Via: eric.hargan@hhs.gov

Re: The failure of the University of Pennsylvania to disclosure the NIH interest in five CAR T patents

Dear Secretary Hargan:

This letter requests that you investigate substantial evidence that the Trustees of the University of Pennsylvania (“UPenn”) failed to satisfy disclosure requirements under the Bayh-Dole Act, 35 U.S.C. §§ 200 *et seq.*, and federal regulations, 37 C.F.R. §§ 401.3(a) & 401.14, with regard to federally-funded subject inventions related to chimeric antigen receptor T cell (“CAR T”) therapy in human cancers such as hematologic malignancies, embodied in the following U.S. Patent Nos.:

8,916,381 (the “381 patent”)
8,975,071 (the “071 patent”)
9,102,760 (the “760 patent”)
9,101,584 (the “584 patent”)
9,102,761 (the “761 patent”)

We have a high degree of confidence that these five patents (collectively, the “2014 patents”) are subject inventions under the Bayh-Dole Act, in that they were “conceived or first actually reduced to practice in the performance of work under a funding agreement.” 35 U.S.C. § 201(e).

In spite of the significant federal funding supporting the chimeric antigen receptor research at UPenn, none of the 2014 patents list government rights in the invention, nor the role of National Institutes of Health (NIH) grants in the development of the CAR T technology.

The 13 patents sharing the same 5 inventors

Table 1 provides information on 13 granted patents that mention “chimeric antigen receptor”, are assigned to the Trustees of the University of Pennsylvania, and which have the same 5 inventors — all current or former employees of the University of Pennsylvania.

For these 13 patents, there are 5 and only 5 inventors mentioned on the patent.

- The four patents filed from June 2012 to December 2013 disclosed several NIH grants and federal government rights in the patent.
- The five patents filed from August to December 2014 disclosed no federal funding.
- The four patents filed from December 2015 to January 2016 also disclosed NIH grants and federal government rights in the patents.

The five patents of interest are those filed between August and December 2014 which share the exact same inventors and the exact same earliest priority date. We believe these 5 patents failed to disclose federal rights in the patents.

Table 1: UPenn CAR Patents with the Five Main Inventors

Patent Number	NIH Grants	Date filed	Earliest priority date	Carl H June	Michael D Kalos	Bruce L Levine	Michael C Milone	David L Porter
9,499,629	K24CA11787901, R01CA120409, 1R01CA105216, R01AI057838 and R011113482**	2012-06-14	2010-12-09	Y	Y	Y	Y	Y
8,906,682	K24CA11787901, R01CA120409, 1R01CA105216, R01AI057838 and R011113482**	2013-07-10	2010-12-09	Y	Y	Y	Y	Y
8,911,993	K24CA11787901, R01CA120409, 1R01CA105216, R01AI057838 and R011113482	2013-07-10	2010-12-09	Y	Y	Y	Y	Y

	K24CA11787901, R01CA120409, 1R01CA105216, R01AI057838 and 9,328,156	R011113482**	2013-12-16	2010-12-09	Y	Y	Y	Y	Y
8,916,381	None reported		2014-08-22	2010-12-09	Y	Y	Y	Y	Y
8,975,071	None reported		2014-08-22	2010-12-09	Y	Y	Y	Y	Y
9,102,760	None reported		2014-12-11	2010-12-09	Y	Y	Y	Y	Y
9,101,584	None reported		2014-12-12	2010-12-09	Y	Y	Y	Y	Y
9,102,761	None reported		2014-12-12	2010-12-09	Y	Y	Y	Y	Y
	K24CA11787901, R01CA120409, 1R01CA105216, R01AI057838 and 9,481,728	R011113482**	2015-12-30	2010-12-09	Y	Y	Y	Y	Y
9,464,140	K24CA11787901, R01CA120409, 1R01CA105216, R01AI057838 and R011113482**		2016-01-14	2010-12-09	Y	Y	Y	Y	Y
9,540,445	K24CA11787901, R01CA120409, 1R01CA105216, R01AI057838 and R011113482**		2016-01-14	2010-12-09	Y	Y	Y	Y	Y
9,518,123	K24CA11787901, R01CA120409, 1R01CA105216, R01AI057838 and R011113482**		2016-01-15	2010-12-09	Y	Y	Y	Y	Y

There is one additional relevant patent that has three of the same five inventors, was filed January 15, 2016, and that disclosed funding from six NIH grants.

Table 2: The CAR Patent with 3 of the 5 Inventors

Patent Number	NIH Grants	Date filed	Earliest priority date	Carl H June	Michael D Kalos	Bruce L Levine	Michael C Milone	David L Porter
9,572,836	K24CA11787901, 1R01CA120409, 1R01CA105216, R01AI057838, R011113482** and 1PN2EY016586	2016-01-15	2012-07-13	Y	Y	Y		

We believe that the 2014 patents, which share the exact same inventors and the exact same earliest priority date, have failed to disclose NIH funding and acknowledge U.S. governmental rights in the patents.

Furthermore, we submit evidence, presented below, that the NIH itself has identified at least three NIH grants as related to each of the five 2014 patents.

Why disclosure is important

CAR T technology is a critical development for immunotherapy that relies on the patient's own cells for the treatment of cancer. This type of treatment holds great promise, with multiple companies including, but not limited to, Novartis, Juno, and Gilead focused on bringing products to market.

There is a concern is that CAR T patents will be used to block innovation by competitors. The relationship between Novartis and UPenn suggests commercial interests will play an important role in enforcing any granted patents. The past litigation involving UPenn, Juno, St Jude's Hospital and others is an early indication there are overlapping claims on CAR T patents and the potential for future litigation. In the past, aggressive litigation by Novartis over Chiron patents on the hepatitis C virus delayed introduction of new drugs by several years. After the announcement that Gilead would acquire Kite Pharma, Gilead indicated to KEI that it expects considerable litigation over CAR T patent claims, in part due to overlapping claims.

The pricing of CAR T treatments will be high when monopolies persist. Novartis's opening price of \$475,000 per treatment for Kymriah¹ is an early indication that CAR T prices will be aggressive, placing burdens on Medicare, Medicaid and other federal programs, as well as the private sector payers.

When the federal government has rights in patents under the Bayh-Dole Act, there are opportunities to force less restrictive licensing, as was done on the WARF patents on stem cells and the patents on vaccine manufacturing technologies using reverse genetics.

The Bayh-Dole Act also requires federally-funded inventions to be made "available to the public on reasonable terms."

¹ Gina Kolata, "New Gene-Therapy Treatments Will Carry Whopping Price Tags," *New York Times*, September 11, 2017. Available at <https://www.nytimes.com/2017/09/11/health/cost-gene-therapy-drugs.html>

I. The Bayh-Dole Act Requires Disclosure of Government Rights in Subject Inventions

The Bayh-Dole Act and federal regulations and guidelines make clear several obligations for contractors in the disclosure of government rights in subject inventions, including: (1) a requirement to disclose that federal funding contributed to an invention; (2) NIH contractual requirements for disclosure; and (3) required language to be inserted in patent applications and the patents, stating the role of federal funding and the government's rights.

First, contractors are required to disclose subject inventions discovered with federal funding in a timely manner and with sufficient detail to describe the invention.

Under 35 U.S.C. § 202(c)(1), any contractor that receives funding from the federal government is required to “disclose each subject invention to the Federal agency within a reasonable time after it becomes known to contractor personnel responsible for the administration of patent matters.”

The statute defines a “subject invention” at 35 U.S.C. § 201(e) as “any invention of the contractor conceived or first actually reduced to practice in the performance of work under a funding agreement,” and defines a contractor at 35 U.S.C. § 201(c) as “any person, small business firm, or nonprofit organization that is party to a funding agreement.”

“Funding agreement” is defined at 35 U.S.C. § 201(b) to mean “any contract, grant, or cooperative agreement entered into between any Federal agency, other than the Tennessee Valley Authority, and any contractor for the performance of experimental, developmental, or research work funded in whole or in part by the Federal Government.”

Under 37 C.F.R. § 401.3(a), each federal funding agreement shall contain the “standard patent rights clause” found at 37 C.F.R. § 401.14(a), barring specific circumstances and exceptions.² Subsection (c)(1) of the patent rights clause outlines the disclosure requirements, including a two month time limit on the disclosure of patents and a requirement that the disclosure have sufficient detail.³

37 C.F.R. § 401.14(a)(c)(1)

(c) Invention Disclosure, Election of Title and Filing of Patent Application by Contractor

² The exceptions do not contain reference to the disclosure requirements.

³ Italics in original.

(1) The *contractor* will disclose each subject invention to the *Federal Agency* within two months after the inventor discloses it in writing to *contractor* personnel responsible for patent matters. The disclosure to the *agency* shall be in the form of a written report and shall identify the contract under which the invention was made and the inventor(s). It shall be sufficiently complete in technical detail to convey a clear understanding to the extent known at the time of the disclosure, of the nature, purpose, operation, and the physical, chemical, biological or electrical characteristics of the invention. The disclosure shall also identify any publication, on sale or public use of the invention and whether a manuscript describing the invention has been submitted for publication and, if so, whether it has been accepted for publication at the time of disclosure. In addition, after disclosure to the *agency*, the *Contractor* will promptly notify the *agency* of the acceptance of any manuscript describing the invention for publication or of any on sale or public use planned by the *contractor*.

...

(4) Requests for extension of the time for disclosure, election, and filing under subparagraphs (1), (2), and (3) may, at the discretion of the *agency*, be granted.

Second, in implementing this regulation, the NIH requires contractors to disclose subject inventions via iEdison, an online electronic system for reporting inventions and patents discovered under federal grants, and via HHS Form 568, entitled, "Final Invention Statement and Certification (For Grant or Award)," available at: <https://grants.nih.gov/grants/hhs568.pdf>.

The NIH specifies the required information on an FAQ related to the use of iEdison, and also notes that contractors should disclose the subject invention even if they have, in the past, failed to report the invention within the two month period:⁴

iEdison & Intellectual Property FAQs and Resources

5. What information is required to report a subject invention?

The invention disclosure must include the following information:

- Either the EIR Number, Invention Docket Number, or both.
- Invention Title
- Names of all of the inventors and the institutions with which they are associated
- Invention Report Date

⁴ Available at: https://era.nih.gov/edison/edison_faqs.cfm#VIII5 (accessed Oct. 10, 2017).

-Description of the Invention that must meet the standards set forth per 37 CFR Sec. 401.14 (a)(c)(1):

"... be sufficiently complete in technical detail to convey a clear understanding to the extent known at the time of the disclosure, of the nature, purpose, operation, and the physical, chemical, biological or electrical characteristics of the invention." 37 C.F.R. 401.14(a)(c)(1)"

-Primary Funding Agency

-All funding agreement numbers and names of the funding agencies

- Any publication, on sale or public use of the invention and whether a manuscript describing the invention has been submitted for publication and, if so, whether it has been accepted for publication at the time of disclosure

9. If I upload a patent application, can that patent application satisfy the Invention Disclosure Report requirement?

Yes, so long as the EIR Number or Invention Docket Number is included on the submission, the patent record containing the patent/patent application number has been reported in iEdison, and you upload proof that the patent application was filed with the USPTO, e.g., a USPTO submission receipt.

10. What should a grantee/contractor do if a subject invention hasn't been reported to the awarding agency within the required 2 month period?

Always report the invention, even if it is late. The invention report date should be the date the inventor notified the awardee institution of the subject invention. Provide an explanation in the "Explanatory Notes" section of the invention record.

On February 17, 2016, the NIH issued a notice entitled "Reminder: All Subject Inventions Must Be Reported on the HHS 568 - Final Invention Statement and Certification (For Grant or Award) and in iEdison." The notice explained that failure to disclose the subject invention via both iEdison and Form 568 could result in the loss of rights in the invention.⁵ As explained below in section V on remedies, this notice is consistent with precedent related to failure to disclose.

Finally, under 35 U.S.C. § 202(c)(6) and 37 C.F.R. § 1.77(b)(3), contractors are required to state within the patent application that the federal government contributed funding to support the discovery of the invention and that the government retains certain rights:

⁵ National Institutes of Health, Reminder: All Subject Inventions Must Be Reported on the HHS 568 - Final Invention Statement and Certification (For Grant or Award) and in iEdison, NOT-OD-16-066 (Feb. 17, 2016), NIH Guide Notice, <https://grants.nih.gov/grants/guide/notice-files/NOT-OD-16-066.html>.

35 U.S.C. § 202(c)(6)

(c) Each funding agreement with a small business firm or nonprofit organization shall contain appropriate provisions to effectuate the following:

...

(6) An obligation on the part of the contractor, in the event a United States patent application is filed by or on its behalf or by any assignee of the contractor, to include within the specification of such application and any patent issuing thereon, a statement specifying that the invention was made with Government support and that the Government has certain rights in the invention.

35 C.F.R. § 1.77(b)(3)

(b) The specification should include the following sections in order:

...

(3) Statement regarding federally sponsored research or development.

The Manual of Patent Examining Procedure contains the following recommended language:

"This invention was made with government support under (identify the contract) awarded by (identify the Federal agency). The government has certain rights in the invention."⁶

II. UPenn Failed to Disclose the 2014 Patents as Subject Inventions Under the Bayh-Dole Act

UPenn received substantial federal funding from the NIH for the development of CAR T technology

Seven grants from the NIH between the years of 1995 and 2017 helped push UPenn to the forefront of research institutions working on the development of CAR T technology.

⁶ MPEP (9th ed. Rev. 07.2015, Nov. 2015), § 310.

Table 3a: NIH Grants to UPenn Relating to CAR T Technology

NIH Grant	Grant Period	Grant Title	Patents	Grant Recipient	Grant Amount
1R01CA105216	2004	CULTURE SYSTEMS TO PROPOGATE [sic] HUMAN T CELL SUBSETS	12	JUNE, CARL H.	\$286,100
1R01CA120409	2006	IMMUNOTHERAPY OF MESOTHELIN EXPRESSING TUMORS WITH LENTIVIRAL ENGINEERED T CELLS	2	JUNE, CARL H.	\$278,675
R01CA120409	2006-2016	IMMUNOTHERAPY WITH CAR T CELLS/ IMMUNOTHERAPY OF MESOTHELIN EXPRESSING TUMORS WITH LENTIVIRAL ENGINEERED T CELLS	10	JUNE, CARL H.	\$2,676,065
K24CA11787901	2006	MID-CAREER INVESTIGATOR AWARD IN ALLOGENEIC ADOPTIVE IMMUNOTHERAPY	9	PORTER, DAVID	\$155,592
R01CA172921	2013-2017	USE OF GENETICALLY ENGINEERED T CELLS TARGETING TUMOR STROMA TO TREAT LUNG CANCER	1	ALBELDA, STEVEN MARK	\$1,177,634
R01AI057838	2004-2008	REGULATION OF HUMAN T CELL ACTIVATION BY THE CD28 FAMILY	12	RILEY, JAMES L	\$1,731,361
P01CA66726	1995-2016	IMMUNO/IMMUNO-GENE THERAPIES FOR THORACIC MALIGNANCIES, GENE THERAPY FOR MALIGNANT MESOTHELIOMA	1	ALBELDA, STEVEN MARK et al.	\$22,203,754

In addition, the University of Pennsylvania was co-recipient of one grant with the Wistar Institute:

Table 3b: NIH Grants to UPenn as Co-Recipient Relating to CAR T Technology

NIH Grant	Grant Period	Grant Title	Patents	Grant Recipient	Grant Amount
CA141144	2010-2014	FIBROBLAST ACTIVATION PROTEIN IN THE TUMOR MICROENVIRONMENT IN LUNG CANCER	1	PURE', ELLEN	\$1,573,613

UPenn is the currently the assignee of twenty-nine patents relating to CAR technology

As of the date of this letter, the Trustees of the University of Pennsylvania is the assignee of twenty-nine US patents that include the term "chimeric antigen receptors." The filing dates for the patents are from February 4, 2011 to January 15, 2016. The patents were granted from December 23, 2014 to October 10, 2017.

Thirteen of the twenty-nine patents share the same five inventors, including the 2014 patents

As described at the outset, thirteen of the twenty-nine patents list the same five inventors: Carl H June, Michael D Kalos, Bruce L Levine, Michael C Milone, and David L Porter. A fourteenth patent omits Milone and Porter as inventors, while June, Kalos and Levine remain listed.

As shown in Table 1, of these particular patents with the same five inventors, only the 2014 patents fail to disclose the NIH grants that supported the invention.

Note that of the thirteen patents with the five main inventors, all except the 2014 patents refer to the same grants: K24CA11787901, R01CA120409, 1R01CA105216, R01AI057838 and R011113482**. The fourteenth patent (with three of the five inventors) discloses these same grants in addition to NIH grant 1PN2EY016586.

All thirteen of the patents with these five main inventors have patents with the same earliest priority date of December 09, 2010. The 2014 patents in particular were filed on August 22 and December 12 of 2014.

The inventors of the 2014 patents

Carl H. June, M.D.

Carl H. June is the Richard W. Vague Professor in Immunotherapy, Director of the Center for Cellular Immunotherapies, and Director of the Parker Institute for Cancer Immunotherapy at the University of Pennsylvania's Perelman School of Medicine. He is the director of Translational Research at the Abramson Cancer Center as well as an investigator of the Abramson Family Cancer Research Institute. His lab researches and develops CARs and the means to deliver them into human T cells.⁷ Dr. June has been examining T cell systems and CAR therapies for several decades, and has published extensively on the topics. In July 2014, his lab's CAR T approach to cancer immunotherapy received US FDA Breakthrough Therapy designation, the first academic research center to receive such a recognition. In 2017 Dr. June received the

⁷ <http://www.med.upenn.edu/apps/faculty/index.php/g275/p2328>

David A. Karnofsky Memorial Award for his role in developing engineered T cells in targeted cancer therapy. Dr. June became tenured faculty at UPenn in 1999.⁸

Michael D. Kalos, PhD

Michael D. Kalos is the Chief Scientific Officer in Cancer Immunobiology at Eli Lilly and Company, but was a faculty member at the University of Pennsylvania from 2008 to 2013, where he established the Translational and Correlative Studies Laboratory within the Perelman School of Medicine.⁹

Michael Milone

Michael Milone is an Associate Professor of Pathology and Laboratory Medicine at the Hospital of the University of Pennsylvania and Perelman School of Medicine.¹⁰ Milone's LinkedIn entry notes that as a postdoctoral fellow working with Dr. Carl June, Milone "designed CTL019 (TN: Kymriah, INN: tisagenlecleucel), a CD19-specific T cell immunotherapy, and conducted the IND-enabling, pre-clinical studies of this novel genetically-engineered cell therapy required for the initial Phase I clinical trial."¹¹ His current research includes, "developing chimeric antigen receptors (CARs) for adoptive immunotherapy of cancer with enhanced function and improved safety, developing and applying synthetic immunoreceptors to the treatment of immune-mediated disease, and exploring the role of co-stimulatory signals in directing T cell metabolism and the way this metabolism affects T cell function within tumors."¹² Dr. Milone has been with the University since 1999.¹³

Bruce Levine

Dr. Bruce Levine is a Barbara and Edward Netter Professor in Cancer Gene Therapy, and is the Founding Director of the Clinical Cell and Vaccine Production Facility (CVPF) in the Department of Pathology and Laboratory Medicine and the Abramson Cancer Center, Perelman School of Medicine, University of Pennsylvania, and has been with the University since 1999.¹⁴ Dr. Levine lists "good manufacturing practices" as an area of expertise in his biography on the UPenn website.¹⁵

⁸ <http://www.aacr.org/Funding/Pages/su2c-cri-committee-detail.aspx?ItemID=2#.Wd0TLUuGPq6>

⁹ <https://www.linkedin.com/in/michael-kalos-81366b9>

¹⁰ <http://pathology.med.upenn.edu/department/people/439/michael-c-milone>

¹¹ <https://www.linkedin.com/in/michael-milone-5a251736/>

¹² <http://pathology.med.upenn.edu/department/people/439/michael-c-milone>

¹³ <https://www.linkedin.com/in/michael-milone-5a251736/>

¹⁴ <https://www.linkedin.com/in/bruce-levine-9976859/>

¹⁵ <http://pathology.med.upenn.edu/department/people/291/bruce-l-levine>

David L. Porter

David L. Porter is the Jodi Fisher Horowitz Professor in Leukemia Care Excellence, and Director of Blood and Marrow Transplantation at the Hospital of the University of Pennsylvania.¹⁶ He was with the University at least as early as 2002 when working in the division of Hematology-Oncology.¹⁷ Dr. Porter, as well as Dr. Milone, are also the two clinical collaborators in the Nanomedicine Center for Mechanobiology Directing the Immune Response, which receives funding from the NIH Common Fund.¹⁸

The NIH RePORTER website shows that the 2014 Patents share an identical “Core NIH Project Number” for NIH grant number R01CA105216

The NIH RePORTER website is a tool that “allows users to search a repository of NIH funded research projects”.¹⁹ NIH grant number R01CA105216, entitled “Culture Systems to propagate [sic] Human T cell Subsets” and given to Dr. Carl H. June at the University of Pennsylvania, is connected to 12 patents (see Figure 1). This project was awarded a total of \$1,460,542 from 2004 to 2008 to study antigen presenting cells and T cell subsets for cancer and HIV immunotherapy.

The findings from this project were published in 31 articles found in academic peer-reviewed journals. These findings are related to and support claims from patents listed in Table 2, including 8916381, 8975071, 9102760, 9101584 and 9102761. For example, Dr. June’s lab reported on better ways to culture and grow CAR T cells, and, characterized CARs constructed with multiple intracellular co-stimulatory domains such as CD28 or 4-1BB with CD3zeta.²⁰ These signaling domains are claimed as key parts of the CAR construction in the 2014 patents.

Methods and compositions in the 2014 patents clearly stem from project R01CA105216 and other NIH funded research conducted in Dr. June’s laboratory. Though the NIH reports these patents to be connected to R01CA105216, there is a failure to mention the government interests within the patents.

Figure 1: Screenshot of NIH-RePORTER Results (taken October 10, 2017) of Patents Connected to Grant Number R01CA105216.

¹⁶ <https://www.med.upenn.edu/apps/faculty/index.php/g348/p4492>

¹⁷ https://www.researchgate.net/publication/10953797_Umbilical_cord_blood_transplantation_Where_do_we_stand

¹⁸ <https://commonfund.nih.gov/nanomedicine/devcenters/mechanicalbiology>

¹⁹ <https://projectreporter.nih.gov/reporter.cfm>

²⁰ Frigault MJ et al. Identification of chimeric antigen receptors that mediate constitutive or inducible proliferation of T cells. *Cancer Immunol Res.* Apr 2015 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4390458/#SD1>)

U.S. Department of Health & Human Services

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[ABOUT RePORTER RESULTS](#)

Grant ID/Reference Number	Patent Number	Title	Patent Office	Funding Agency
R01CA105216	7,754,482	Artificial antigen presenting cells and uses therefor	UNIVERSITY OF PENNSYLVANIA	NID
R01CA105216	8,722,400	Artificial antigen presenting cells and uses therefor	UNIVERSITY OF PENNSYLVANIA	NID
R01CA105216	9,906,793	Composition for treatment of cancer	UNIVERSITY OF PENNSYLVANIA	NID
R01CA105216	9,906,790	Composition for treatment of cancer	UNIVERSITY OF PENNSYLVANIA	NID
R01CA105216	8,906,773	Composition for treatment of cancer	UNIVERSITY OF PENNSYLVANIA	NID
R01CA105216	8,906,993	Composition for treatment of cancer	UNIVERSITY OF PENNSYLVANIA	NID
R01CA105216	9,933,438	K24 antibody mycokeratins for prevention and treatment of immunotherapy human T-cell cancers	UNIVERSITY OF PENNSYLVANIA	NID
R01CA105216	9,972,696	Methods for assessing the availability of recombinant T-cells for administration	UNIVERSITY OF PENNSYLVANIA	NID
R01CA105216	8,916,381	Methods for treatment of cancer	UNIVERSITY OF PENNSYLVANIA	NID
R01CA105216	9,916,584	Methods for treatment of cancer	UNIVERSITY OF PENNSYLVANIA	NID
R01CA105216	8,906,682	Methods for treatment of cancer	UNIVERSITY OF PENNSYLVANIA	NID
R01CA105216	8,906,156	Methods for treatment of cancer	UNIVERSITY OF PENNSYLVANIA	NID

Table 4 presents the 12 patents in the RePorter search for NIH grant R01CA105216. The patents with a blue background are the 2014 patents.

Table 4: The RePorter Designated Patents for Grant R01CA105216

NIH Grant	Patent	Title	Grantee	Federal rights disclosed on patent
R01CA105216	7,754,482	Artificial antigen presenting cells and uses therefor	UNIVERSITY OF PENNSYLVANIA	R21 AI060477, R01 CA105216 R01 AI 057838
R01CA105216	8,722,400	Artificial antigen presenting cells and uses therefor	UNIVERSITY OF PENNSYLVANIA	R21 AI060477, R01 CA105216 R01 AI057858
R01CA105216	8,906,682	Methods for treatment of cancer	UNIVERSITY OF PENNSYLVANIA	K24 CA11787901, R01CA120409, 1R01CA105216,

				RO1AI057838 RO11113482
R01CA105216	8,911,993	Compositions for treatment of cancer	UNIVERSITY OF PENNSYLVANIA	K24 CA11787901, R01CA120409, 1RO1CA105216, RO1AI057838 RO11113482
R01CA105216	8,916,381	Methods for treatment of cancer	UNIVERSITY OF PENNSYLVANIA	None
R01CA105216	8,975,071	Compositions for treatment of cancer	UNIVERSITY OF PENNSYLVANIA	None
R01CA105216	9,101,584	Methods for treatment of cancer	UNIVERSITY OF PENNSYLVANIA	None
R01CA105216	9,102,760	Compositions for treatment of cancer	UNIVERSITY OF PENNSYLVANIA	None
R01CA105216	9,102,761	Compositions for treatment of cancer	UNIVERSITY OF PENNSYLVANIA	None
R01CA105216	9,133,436	ICOS critically regulates the expansion and function of inflammatory human Th17 cells	UNIVERSITY OF PENNSYLVANIA	5R01CA105216, 1R01CA120409, 5P01CA066726 R01A1057838
R01CA105216	9,328,156	Use of chimeric antigen receptor-modified T cells to treat cancer	UNIVERSITY OF PENNSYLVANIA	K24 CA11787901, R01CA120409, 1RO1CA105216, RO1AI057838 RO11113482
R01CA105216	9,572,836	Methods for assessing the suitability of transduced T cells for administration	UNIVERSITY OF PENNSYLVANIA	K24 CA11787901, 1PN2-EY016586, 1R01CA105216, 1R01CA120409, RO1AI057838, RO11113482

The NIH RePORTER website shows that the 2014 Patents share an identical “Core NIH Project Number” for NIH grant number R01AI057838

Chimeric antigen receptors are composed of different segments having distinct functions in antigen recognition, signaling and co-stimulation. Understanding the right combination of these segments is important in the function of the CAR and, the activation and survival of the T cell. T cell activation enables these to multiply and allows for the cells to respond to tumors they recognize. The NIH funded project R01AI057838 entitled “Regulation of Human T Cell Activation by the CD28 Family” aims to discern the mechanism behind antigen-dependent signaling pathways responsible for survival and anti-tumor functions so that clinicians can better control therapeutic T cells. Specifically this project studies signaling and activation through

CD28 and ICOS. The R01AI057838 grant is connected to 12 patents including the 2014 patents. Embodiments of second generation CARs described in the 2014 patents incorporate co-stimulatory fragments, such as CD28 and ICOS, into their intracellular domains. Additionally, published results relevant to the 2014 patents appear in articles supported by the R01AI057838 grant. Scientific articles of particular interest are; "Chimeric receptors containing CD137 signal transduction domains mediate enhanced survival of T cells and increased antileukemic efficacy in vivo", "The inducible costimulator (ICOS) is critical for the development of human T(H)17 cells" and "CD28 costimulation is essential for human T regulatory expansion and function".^{21, 22, 23} The R01AI057838 project grant was awarded to Dr. James L Riley at University of Pennsylvania, from 2004 to 2008. The total amount of funding for these four years was \$1,731,361.²⁴

Figure 2: Screenshot of NIH-RePORTER Results (taken October 11, 2017) of Patents Connected to Grant Number R01AI057838.

The screenshot shows a search results page for NIH-RePORTER. The top navigation bar includes links for Projects, Publications, Grants, Clinical Studies, Data & Visualizations, Map, News & More. Below the navigation is a search bar with placeholder text 'Search RePORTER' and a 'SEARCH' button. A 'REFRESH' button is also present. The main content area is titled 'Search Results' and displays a table of 12 patent records. The table has columns for 'Grant Number', 'Patent Number', 'Title', 'Inventor(s)', and 'Primary Agency'. All 12 patents listed are from the University of Pennsylvania and are managed by NIH. The patents are all related to 'Artificial antigen-presenting cells and uses thereof' or 'Compositions for treatment of cancer'.

Grant Number	Patent Number	Title	Inventor(s)	Primary Agency
R01AI057838	7754662	Artificial antigen-presenting cells and uses thereof	UNIVERSITY OF PENNSYLVANIA	NIH
R01AI057838	8721469	Artificial antigen-presenting cells and uses thereof	UNIVERSITY OF PENNSYLVANIA	NIH
R01AI057838	8875071	Compositions for treatment of cancer	UNIVERSITY OF PENNSYLVANIA	NIH
R01AI057838	9102781	Compositions for treatment of cancer	UNIVERSITY OF PENNSYLVANIA	NIH
R01AI057838	9301993	Compositions for treatment of cancer	UNIVERSITY OF PENNSYLVANIA	NIH
R01AI057838	9102780	Compositions for treatment of cancer	UNIVERSITY OF PENNSYLVANIA	NIH
R01AI057838	9334335	ICOS antibody mediates the expansion and function of effector memory T cells	UNIVERSITY OF PENNSYLVANIA	NIH
R01AI057838	9672838	Methods for assessing the subsets of naïve/naïf T cells for expansion	UNIVERSITY OF PENNSYLVANIA	NIH
R01AI057838	8863081	Methods for treatment of cancer	UNIVERSITY OF PENNSYLVANIA	NIH
R01AI057838	8901064	Methods for treatment of cancer	UNIVERSITY OF PENNSYLVANIA	NIH
R01AI057838	8906682	Methods for treatment of cancer	UNIVERSITY OF PENNSYLVANIA	NIH
R01AI057838	9328156	Use of different adjuvants to expand modified T cells to treat cancer	UNIVERSITY OF PENNSYLVANIA	NIH

²¹ Milone MC et al. Chimeric receptors containing CD137 signal transduction domains mediate enhanced survival of T cells and increased antileukemic efficacy in vivo. Mol Ther. Aug 2009

²² Paulos CM et al. The inducible costimulator (ICOS) is critical for the development of human T(H)17 cells. Sci Transl Med. Oct 2010

²³ Golovina TN et al. CD28 costimulation is essential for human T regulatory expansion and function. J Immunol. Aug 2008

²⁴ <https://projectreporter.nih.gov>

We checked the patent disclosures on the twelve patents identified by RePorter as relevant to NIH Grant R01A1057838. As reported in Table 5, all disclosed federal funding except for the five “2014” patents.

Table 5: The 12 RePorter-Designated Patents for Grant R01A1057838

NIH Grant	Patent	Title	Grantee	Federal rights disclosed on patent
R01AI057838	9,572,836	Methods for assessing the suitability of transduced T cells for administration	UNIVERSITY OF PENNSYLVANIA	K24 CA11787901, 1PN2-EY016586, 1R01CA105216, 1R01CA120409, RO1AI057838, R01113482,
R01AI057838	9,328,156	Use of chimeric antigen receptor-modified T cells to treat cancer	UNIVERSITY OF PENNSYLVANIA	K24 CA11787901, R01CA120409, 1R01CA105216, RO1AI057838, R01113482
R01AI057838	9,133,436	ICOS critically regulates the expansion and function of inflammatory human Th17 cells	UNIVERSITY OF PENNSYLVANIA	5R01CA105216, 1R01CA120409, 5P01CA066726, R01A1057838
R01AI057838	9,102,761	Compositions for treatment of cancer	UNIVERSITY OF PENNSYLVANIA	None
R01AI057838	9,102,760	Compositions for treatment of cancer	UNIVERSITY OF PENNSYLVANIA	None
R01AI057838	9,101,584	Methods for treatment of cancer	UNIVERSITY OF PENNSYLVANIA	None
R01AI057838	8,975,071	Compositions for treatment of cancer	UNIVERSITY OF PENNSYLVANIA	None
R01AI057838	8,916,381	Methods for treatment of cancer	UNIVERSITY OF PENNSYLVANIA	None
R01AI057838	8,911,993	Compositions for treatment of cancer	UNIVERSITY OF PENNSYLVANIA	K24 CA11787901, R01CA120409, 1R01CA105216, RO1AI057838, R01113482
R01AI057838	8,906,682	Methods for treatment of cancer	UNIVERSITY OF PENNSYLVANIA	K24 CA11787901, R01CA120409, 1R01CA105216, RO1AI057838, R01113482
R01AI057838	8,722,400	Artificial antigen presenting cells and	UNIVERSITY OF	R21 AI060477,

		uses therefor	PENNSYLVANIA	R01 CA105216, R01 AI057858.
R01AI057838	7,754,482	Artificial antigen presenting cells and uses therefor	UNIVERSITY OF PENNSYLVANIA	R21 AI060477, R01 CA105216, R01 AI 057838

The NIH RePORTER website shows that the 2014 Patents share an identical “Core NIH Project Number” for NIH grant number K24CA117879

Nine patents, including the 2014 patents, are affiliated with the K24CA117879 “Mid-career Investigator Award in Allogeneic Adoptive Immunotherapy” project (Figure 3). Dr. David Porter, from the University of Pennsylvania, was awarded \$777,980 between 2006 and 2010, to conduct research under this project. K42 mid-career grants are awarded to clinicians for “patient-oriented research”.²⁵ The research conducted under this grant applied to cellular immunotherapy against cancer. Importantly, grant K24CA117879 supported the crucial but small 2011 UPenn clinical study with Dr. June, “Chimeric Antigen Receptor–Modified T Cells in Chronic Lymphoid Leukemia” (NCT01029366) that demonstrated the potential of their CAR T cell therapy in leukemia. Shortly after this study, Novartis gave UPenn funding towards a research center in exchange for exclusive worldwide rights to CARs developed at UPenn.²⁶

Figure 3: Screenshot of NIH-RePORTER Results (taken October 11, 2017) of Patents Connected to Grant Number K24CA117879.

Search Results

ABOUT REPORTER RESULTS

There were 9 connections of patents to projects matching your search criteria. Click on the column header to sort the results.

Grant Number	Patent Number	Patent Title	Patent Owner	Primary Assignee
K24CA117879	8811993	Compositions for treatment of cancer	UNIVERSITY OF PENNSYLVANIA	NIH
K24CA117879	8975071	Compositions for treatment of cancer	UNIVERSITY OF PENNSYLVANIA	NIH
K24CA117879	8162760	Compositions for treatment of cancer	UNIVERSITY OF PENNSYLVANIA	NIH
K24CA117879	8162761	Compositions for treatment of cancer	UNIVERSITY OF PENNSYLVANIA	NIH
K24CA117879	9572036	Methods for assessing the suitability of transduced T cells for anti-tumor effects	UNIVERSITY OF PENNSYLVANIA	NIH
K24CA117879	8162194	Methods for treatment of cancer	UNIVERSITY OF PENNSYLVANIA	NIH
K24CA117879	8816081	Methods for treatment of cancer	UNIVERSITY OF PENNSYLVANIA	NIH
K24CA117879	8906682	Methods for treatment of cancer	UNIVERSITY OF PENNSYLVANIA	NIH
K24CA117879	8828158	Use of chimeric antigen receptor-modified T cells to treat cancer	UNIVERSITY OF PENNSYLVANIA	NIH

²⁵ https://grants.nih.gov/grants/funding/funding_program.htm

²⁶ <https://www.elsevier.com/connect/penn-and-novartis-collaborate-on-new-cancer-drug>

We checked the patent disclosures on the nine patents identified by RePorter as relevant to NIH Grant **K24CA117879**. As reported in Table 6, all disclosed federal funding exception for the five “2014” patents.

Table 6: The 9 RePorter Designated Patents for Grant K24CA117879.

NIH Grant	Patent	Title	Grantee	Federal rights disclosed on patent
K24CA117879	9572836	Methods for assessing the suitability of transduced T cells for administration	UNIVERSITY OF PENNSYLVANIA	K24 CA11787901, 1PN2-EY016586, 1R01CA105216, 1R01CA120409, RO1AI057838, R01113482
K24CA117879	9328156	Use of chimeric antigen receptor-modified T cells to treat cancer	UNIVERSITY OF PENNSYLVANIA	K24 CA11787901, R01CA120409, 1R01CA105216, RO1AI057838, R01113482
K24CA117879	9102761	Compositions for treatment of cancer	UNIVERSITY OF PENNSYLVANIA	None
K24CA117879	9102760	Compositions for treatment of cancer	UNIVERSITY OF PENNSYLVANIA	None
K24CA117879	9101584	Methods for treatment of cancer	UNIVERSITY OF PENNSYLVANIA	None
K24CA117879	8975071	Compositions for treatment of cancer	UNIVERSITY OF PENNSYLVANIA	None
K24CA117879	8916381	Methods for treatment of cancer	UNIVERSITY OF PENNSYLVANIA	None
K24CA117879	8911993	Compositions for treatment of cancer	UNIVERSITY OF PENNSYLVANIA	K24 CA11787901, R01CA120409, 1R01CA105216, RO1AI057838, R01113482
K24CA117879	8906682	Methods for treatment of cancer	UNIVERSITY OF PENNSYLVANIA	K24 CA11787901, R01CA120409, 1R01CA105216, RO1AI057838, R01113482

III. In the Case of a Failure to Disclose, the Government May Reclaim the Invention

Failure to disclose subject inventions pursuant to 35 U.S.C. § 202(c)(1) permits the Federal Government to “receive title to any subject invention not disclosed to it within such time” (emphasis added).

In the past, the federal government has utilized its authority to claim title in subject inventions that have not been properly disclosed, as in the case of *Campbell Plastics Engineering & Mfg., Inc. v. Brownlee*, 389 F.3d 1243 (Fed. Cir. 2004) (finding that federal government claim of title in invention was legitimate under federal acquisition regulations and supported by the Bayh-Dole Act where disclosure submissions were “piecemeal” and violated the contractual agreement with the government); see also *Central Admixture Pharmacy Services, Inc. v. Advanced Cardiac Solutions, P.C.*, 482 F.3d 1347, 1352-53 (Fed. Cir. 2007) (“Critically, *Campbell Plastics* holds that a Bayh–Dole violation grants the government *discretionary* authority to take title. . . . When a violation occurs, the government can choose to take action; thus, title to the patent may be voidable.”).

In *Campbell Plastics*, the court found that the contract was clear and unambiguous, but moreover the government’s claim to title was “buttressed by the policy considerations behind the Bayh-Dole Act.” *Id.* at 1248. These include, specifically under 35 U.S.C. § 200, the need “to ensure that the Government obtains sufficient rights in federally supported inventions to meet the needs of the Government and protect the public against nonuse or unreasonable use of inventions.”

IV. Conclusion

We believe that there is sufficient evidence to warrant an investigation into this matter. If the 2014 patents are subject inventions under the Bayh-Dole Act, UPenn has an affirmative obligation to disclose the inventions to the government and to explicitly state the government’s rights in the patents. The 2014 patents appear to have failed to do so in spite of the abundant evidence suggesting that they are subject inventions.

The failure to disclose government rights in a subject invention does a disservice to taxpayers, consumers and patients.

We request a meeting at your earliest convenience to discuss this matter in further detail.

Sincerely,



James Love
Director
Knowledge Ecology International
james.love@keionline.org



Andrew S. Goldman, Esq.
Counsel, Policy and Legal Affairs
andrew.goldman@keionline.org



Diane Singhroy
Scientific and Technical Advisor
diane.singhroy@keionline.org

Cc:

Gary M. Beck, Advisor for External Affairs, HHS
Ann Hammersla, Director of OPERA's Division of Extramural Inventions and Technology
Resources, NIH

From: Berkson, Laura (NIH/OD) [E] [/O=NIH/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=DAMIANOLD]
Sent: 9/6/2016 4:59:56 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=OD/cn=ROHRBAUM]
Subject: BRAIN entries
Attachments: Drug Pricing BRAIN entry.docx; Durbin Xtandi QA BRAIN entry.docx

Here they are. Let me know if you need anything else.

b5

From: Hammersla, Ann (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/CN=RECIPIENTS/CN=HAMMERSLAA]
Sent: 6/14/2017 2:51:49 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=OD/cn=ROHRBAUM]
Subject: Dft Response
Attachments: KEI Response 06142017ah.docx

Mark: Attached is my draft of the response to KEI on the CRISPR technology. Let me know what your edits are.

Ann

--
Ann M. Hammersla, J.D.
Director
Division of Extramural Inventions and Technology Resources
Office of Policy for Extramural Research Administration
Rockledge 1, Suite 310
6705 Rockledge Drive
Bethesda, Maryland 20892-7974
PHONE: 301-435-0745

b5

b5

From: Rodriguez, Richard (NIH/NCI) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=8092CB5394E04733AC0D4D84D25F65E5-RODRIGR]
Sent: 11/7/2017 6:13:27 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718ccb29fab-rohrbaum]
Subject: RE: responses to FRNs

Hi again,

A pretty quick response from NCI staff. KEI and Sara Elizabeth Siegler routinely ask these types of questions. I can provide examples if you like, so please let me know.

Richard

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Tuesday, November 7, 2017 10:39 AM
To: Rodriguez, Richard (NIH/NCI) [E] <richard.rodriguez@nih.gov>
Subject: responses to FRNs

Richard:

Do you recall our receiving questions from a FRN notice not directly related to the technology and the license, such as how much money was spent in developing this technology, or did this company receive government funding?

How was this handled or how are you handling it now?

Thx

Mark L. Rohrbaugh, Ph.D., J.D.
Special Advisor for Technology Transfer
Director, Division of Technology Transfer and Innovation Policy
Office of Science Policy
Office of the Director
National Institutes of Health

From: Berkley, Dale (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=5EE461C29F5045A49F0ADF82CAAA2F31-BERKLEYD]
Sent: 10/11/2018 3:16:30 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
CC: Johnson, Melanye (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=b411f6afb47f4a7b807818717147115e-johnsonmk]
Subject: FW: KEI v. NIH
Attachments: 5.1--Memorandum of Law--6.8.2018.pdf; 9--RESPONSE in Opposition re 5--6.25.2018.pdf

Mark—in case you will be in town next Monday the 15th. I will be out of town that day and an oral hearing for the KEI case has unexpectedly remained on the calendar, so the AUSA (Alan Lazerow) is going to have to argue our Motion to Dismiss on Monday. Melanye will be there in my place.

If you have any interest in attending the hearing in Greenbelt, here is the location of the court where the hearing will take place. Attached is the government's memorandum and KEI's response.

Thanks, Dale

10:00 AM Motions Hearing
Knowledge Ecology v. National Institutes of Health
PJM 18cv1130
Courtroom: 4A

6500 Cherrywood Lane
Greenbelt, MD 20770
(301) 344-0660

Dale D. Berkley, Ph.D., J.D.
Office of the General Counsel, PHD, NIH Branch
Bldg. 31, Rm. 47
Bethesda, MD 20892
301-496-6043
301-402-2528(Fax)

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**IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MARYLAND**

KNOWLEDGE ECOLOGY
INTERNATIONAL,

Plaintiff,

v.

NATIONAL INSTITUTES OF HEALTH, *et
al.*,

Defendants.

Case No. 8:18-cv-01130-PJM

MEMORANDUM IN SUPPORT OF MOTION TO DISMISS

Defendants, National Institutes of Health (“NIH”), National Cancer Institute (“NCI”), Francis S. Collins (“Collins”), and David Lambertson (“Lambertson,” and together with NIH, NCI, and Collins, the “Defendants”), by and through their counsel, Robert K. Hur, United States Attorney for the District of Maryland, and Alan C. Lazerow, Assistant United States Attorney for that district, respectfully submits this *Memorandum in Support of Motion to Dismiss*.

I. INTRODUCTION

By the *Complaint for Declaratory, Injunctive, and Other Relief*, see ECF No. 1 (the “Complaint”), Knowledge Ecology International (“KEI” or the “Plaintiff”), a public-interest organization, challenges NIH’s grant of an exclusive license for technology relating to certain cancer treatments to a large pharmaceutical company. The Court need not address the merits of Plaintiff’s contentions, because Plaintiff lacks standing to bring this suit.

First, because Plaintiff does not allege what injuries KEI will suffer because of Defendants’ alleged conduct, Plaintiff lacks what the caselaw has coined “organizational standing.” And because Plaintiff does not allege that the patients, taxpayers, and consumers Plaintiff purports to represent control KEI’s functions, elect or serve on KEI’s leadership, or finance KEI’s activities,

Plaintiff lacks “associational standing” to sue on behalf of its purported constituents. For these reasons, and as explained more fully below, the Court should dismiss the Complaint for lack of subject-matter jurisdiction, under Rule 12(b)(1) of the Federal Rules of Civil Procedure (the “Rules”).

II. **FACTS**

A. **THE PROPOSED LICENSE**

Through its technology transfer program, NIH makes patents and other intellectual property owned by the United States available to public and private companies, through the granting of exclusive and non-exclusive licenses to use that technology. Declaration of Dale D. Berkley, Ph.D., J.D. (the “Berkley Declaration”)¹ ¶ 2. Licenses granted through the technology transfer program, in almost all cases, require the licensees to pay royalties to the United States. *Id.* ¶ 3. Royalties obtained through licensing provide a return to NIH that supports further research and provide compensation to government employee inventors. *Id.*

On December 20, 2017, NIH posted a notice of intent (the “Notice of Intent”) in the Federal Register regarding the proposed grant of an exclusive license to Kite Pharma, Inc. (“Kite”) for CAR T technology for the treatment of cancer (the “Proposed License”). *See* 82 Fed. Reg. 60406, 60407 (Dec. 20, 2017); Complaint ¶ 47. The Notice of Intent provided that “the public may file comments or objections,” relating to the Proposed License, and that “the prospective exclusive license may be granted unless, within fifteen (15) days from the date of this published notice, [NCI] receives written evidence and argument that establishes that the grant of the license would

¹ A copy of the Berkley Declaration is attached as **Exhibit A**.

not be consistent with the requirements of 35 U.S.C. 209 and 37 CFR part 404.” 82 Fed. Reg. 60406, 60407.

B. PLAINTIFF OPPOSES THE LICENSE

On January 4, 2018, James Love – apparently affiliated with KEI – wrote to Collins and Lambertson to “express [KEI’s] opposition to the [P]roposed [License].” Berkley Declaration ¶ 6.² Mr. Love attached a five-page document outlining KEI’s opposition to the Proposed License. *Id.* On January 25, 2018, Lambertson responded to Mr. Love by email and attached a response, explaining that “[w]hile your comments have been given full consideration, they do not persuade us that the [Proposed License] would be inconsistent with the regulations and, furthermore, advance public health.” *Id.* ¶ 7.³

On February 14, 2018, Andrew Goldman – also with KEI, and counsel of record for KEI – emailed Collins and Lambertson asking about KEI’s appeal rights, asking Collins and Lambertson to “let [KEI] know what formal procedures the NIH requires for these appeals” *Id.* ¶ 8.⁴ On February 26, 2018, Lambertson responded to Mr. Goldman, noting that under 37 C.F.R. § 404.1(a)(3), an appeal can be taken by only “a person who can demonstrate to the satisfaction of the agency that such person may be damaged by the action,” that NIH “determined

² A copy of the January 4, 2018 email from Mr. Love to Collins and Lambertson, with an attachment, is attached as **Exhibit 1** to the Berkley Declaration.

³ A copy of the January 25, 2018 email from Lambertson to Mr. Love, with an attachment, is attached as **Exhibit 2** to the Berkley Declaration.

⁴ A copy of the February 14, 2018 email from Mr. Goldman to Collins and Lambertson is attached as **Exhibit 3** to the Berkley Declaration.

that there is no likelihood that KEI will be damaged by the agency action,” and that NIH “will not entertain an appeal of our decision.” *Id.* ¶ 9.⁵

Undeterred, also on February 26, 2018, Mr. Goldman responded to Collins and Lambertson, attaching KEI’s appeal of NIH’s response to KEI’s opposition to the Proposed License. *Id.* ¶ 10.⁶ In the attached appeal, KEI represented that it is “a public interest organization” that “represents taxpayers and patients, including cancer patients, who are stakeholders in the outcome of the NIH decision,” and also stated that KEI “represents persons who will be damaged by the decision to proceed with [the Proposed License]” *Id.*

C. THE COMPLAINT

On April 19, 2018, Plaintiff filed the Complaint. Count I of the Complaint asserts a violation of the Federal Property and Administrative Services Act and 5 U.S.C. 706(2)(A), alleging that NIH’s failure “to seek and obtain the antitrust advice of the Attorney General prior to the disposal of federal property to private interests” “is a violation of 40 U.S.C. § 559 and applicable regulations, and constitutes agency action that is arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with the law under 5 U.S.C. § 706(2)(A), or that is illegal agency action under 5 U.S.C. § 706(1).” Complaint ¶¶ 61, 65. Count II of the Complaint asserts a violation of 37 C.F.R. § 404.11 and 5 U.S.C. 706(2)(A), alleging that “Defendants have refused to entertain the rightful appeal of KEI without explanation,” and that such denial “constitutes a violation of 37 C.F.R. § 404.11, as well as an agency action that is arbitrary, capricious, an abuse

⁵ A copy of the February 26, 2018 email from Lambertson to Mr. Goldman is attached as Exhibit 4 to the Berkley Declaration.

⁶ A copy of the February 26, 2018 email from Mr. Goldman to Collins and Lambertson, with attachments, is attached as Exhibit 5 to the Berkley Declaration.

of discretion, or otherwise not in accordance with the law under 5 U.S.C. § 706(2)(A), or that is illegal agency action under 5 U.S.C. § 706(1).” Complaint ¶¶ 69, 70.

In addition to seeking a declaration of the violations above, by the Complaint, Plaintiff seeks to “[i]nvalidate the exclusive license of the NCI CAR technology to Kite,” and asks the Court to “enter appropriate preliminary and permanent injunctive relief to ensure that Defendants comply with FPASA and specifically to ensure that Defendants and their agents take no further actions toward proceeding with the challenged license until they have complied with FPASA and granted KEI the right of appeal.” Complaint at p. 17.

D. PLAINTIFF’S ALLEGATIONS BEARING ON STANDING

As explained below, Plaintiff bears the burden of establishing that it has standing to bring this lawsuit. Thus, a review of Plaintiff’s allegations in the Complaint bearing on standing is appropriate. *See Henley v. Cleveland Bd. of Educ.*, No. 1:10-cv-00431, 2010 WL 796835, at *2 (N.D. Ohio Mar. 3, 2010) (“When a court considers whether a plaintiff has standing to pursue preliminary relief, standing is determined by analyzing the material allegations in the complaint”); *see also BayFirst Solutions, LLC v. United States*, 104 Fed. Cl. 493, 501 (Fed. Cl. 2012) (“Standing, this court has typically held, is predicated on an initial review of the complaint and the allegations therein.”).

Plaintiff alleges that it “is an award-winning nonprofit organization that works extensively on issues pertaining to access to affordable medicines and related intellectual concerns.” Complaint ¶ 5. Plaintiff “conducts research, writing and advocacy in the public interest on behalf of patients, taxpayers, and consumers, including on the licensing of federally-funded and/or federally-owned medical technologies, and comments frequently on proposed exclusive licenses” *Id.* Plaintiff “maintains multiple email lists on ... public health issues for patients, taxpayers,

and consumers, academics, and other interested persons” *Id.* Plaintiff maintains an “IP-Health’ listserv of approximately 2400 subscribers.” *Id.*

Plaintiff alleges that the relief it seeks “would redress actual, concrete injuries to Plaintiff and the patients, taxpayers and consumers Plaintiff represents” *Id.* ¶ 14. In Plaintiff’s view, Defendants’ actions are “an affront to patients, payments, and consumers ... who will be damaged by the higher prices stemming from [the Proposed License]” *Id.* ¶ 72; *see id.* ¶ 1 (mentioning “Defendants’ waste of taxpayer funds that will result in the denial of affordable cancer treatments for patients”).

III. APPLICABLE LEGAL STANDARD: MOTION TO DISMISS FOR LACK OF SUBJECT-MATTER JURISDICTION

As explained below, Defendant maintains that Plaintiff lacks standing to bring this suit. Dismissal under Rule 12(b)(1) is appropriate under such circumstances. *See Zaycer v. Sturm Foods, Inc.*, 896 F. Supp. 2d 399, 403 (D. Md. 2012) (“Under Rule 12(b)(1), if a party lacks standing the court automatically lacks subject matter jurisdiction.”); *McInnes v. Lord Baltimore Employee Retirement Income Account Plan*, 823 F. Supp. 2d 360, 362 (D. Md. 2011) (“Because standing is an element of subject matter jurisdiction, a defendant’s motion to dismiss for lack of standing should be treated under Rule 12(b)(1).”).

As this Court has explained:

A challenge to standing may take two forms: a facial challenge, asserting that the allegations pleaded in the complaint are insufficient to establish standing, or a factual challenge asserting that the jurisdictional allegations of the complaint are not true, or that other facts, outside the four corners of the complaint preclude the exercise of subject matter jurisdiction.

Franklin v. Jackson, No. 8:14-cv-00497, 2015 WL 1186599, at *8 (D. Md. Mar. 3, 2015) (internal quotation marks and modifications omitted). Defendants contend that the allegations in the

Complaint cannot establish Plaintiff's standing. "When analyzing a facial challenge, the court determines whether the allegations in the Complaint, taken as true, are sufficient to establish standing under the plausibility standard of Rule 12(b)(6) and *Iqbal/Twombly*." *Allah-Mensah v. Law Office of Patrick M. Connelly, P.C.*, No. 8:16-cv-01053, 2016 WL 6803775, at *2 (D. Md. Nov. 17, 2016).

A motion to dismiss based on lack of subject-matter jurisdiction, under Rule 12(b)(1), raises whether the court has the competence or authority to hear and decide a particular case. See *Davis v. Thompson*, 367 F. Supp. 2d 792, 299 (D. Md. 2005). As a result, the court "generally may not rule on the merits of a case without first determining that it has the jurisdiction over the category of claim in suit (subject-matter jurisdiction)." *Sinochem Int'l Co. Ltd. v. Malaysia Int'l Shipping Corp.*, 549 U.S. 422, 430-31 (2007) (citing *Steel Co. v. Citizens for a Better Env't*, 523 U.S. 83, 93-102 (1998)). The plaintiff bears the burden of proving that subject-matter jurisdiction exists, including proving that it has standing to sue. See *McInnes*, 823 F. Supp. 2d at 362 ("The plaintiff in a federal action bears the burden of demonstrating that he possesses standing to pursue his claims in federal court.").

The requirement that a plaintiff establish subject-matter jurisdiction "as a threshold matter 'spring[s] from the nature and limits of the judicial power of the United States' and is 'inflexible and without exception.'" *Steel Co.*, 523 U.S. at 95 (some internal quotation marks omitted). For that reason, "[t]he objection that a federal court lacks subject-matter jurisdiction ... may be raised by a party, or by a court on its own initiative, at any stage in the litigation, even after trial and the entry of judgment." *Arbaugh v. Y & H Corp.*, 546 U.S. 500, 506 (2006) (citing Rule 12(h)(3)).

**IV. ARGUMENT: THE COURT SHOULD DISMISS THE COMPLAINT, AS
PLAINTIFF LACKS STANDING**

“An organization may establish standing under two theories: either (a) standing in its own right, or organizational standing, or (b) representational, also known as ‘associational,’ standing based on the fact that members it represents have been harmed.” *Equal Rights Ctr. v. Camden Prop. Trust*, No. 8:07-cv-02357, 2008 WL 8922896, at *5 (D. Md. Sept. 22, 2008). Because Plaintiff asserts that it “brings this action on its own behalf and on behalf of the adversely affected patients and taxpayers that the organization represents,” Complaint ¶ 5, this case implicates both organizational and associational standing. As explained below, Plaintiff lacks both.

A. BECAUSE PLAINTIFF DOES NOT ALLEGE THAT IT HAS OR WILL SUFFER HARM FROM THE PROPOSED LICENSE, PLAINTIFF LACKS ORGANIZATIONAL STANDING

“An organizational plaintiff suing on its own behalf, like an individual, must satisfy the familiar elements of injury-in-fact, causation, and redressability to establish Article III standing.”⁷ *Retail Indus. Leaders Ass’n v. Fielder*, 475 F.3d 180, 186 (4th Cir. 2007); *see Havens Realty Corp. v. Coleman*, 455 U.S. 363, 378 (1982) (“In determining whether [an organizational plaintiff] has standing . . . , we conduct the same inquiry as in the case of an individual.”).

Plaintiff purports to “bring this action on its own behalf,” and asserts that “[t]he requested relief would redress actual, concrete injuries to Plaintiff” Complaint ¶¶ 5, 14. But the Complaint is silent about what “actual” or “concrete” injuries KEI will suffer because of Defendants’ alleged conduct. To be sure, Plaintiff complains of “the denial of affordable cancer

⁷ If a plaintiff has Article III standing, it must also show that it has prudential standing to sue. Here, because Plaintiff lacks Article III standing, the Court need not address prudential standing. *See, e.g., Greenberg v. Bush*, 150 F. Supp. 2d 447, 455 (E.D.N.Y. 2001) (“Because Plaintiffs have not satisfied the threshold Article III standing requirements, the court need not analyze prudential standing considerations.”).

treatment for patients,” Complaint ¶ 1 (emphasis added), the “mismanage[ment of] taxpayer funds,” *id.* ¶ 4 (emphasis added), while referencing the “adversely affected patients and taxpayers,” *id.* ¶ 5 (emphasis added), and the asserted “affront to patients, taxpayers, and consumers” *Id.* ¶ 72 (emphasis added). But these asserted harms purport to inure to the detriment of cancer patients, taxpayers,⁸ and consumers – not to KEI. And although Defendants’ asserted conduct may, in some way, implicate KEI’s institutional goals and purposes, “institutional goals and purposes cannot sustain federal standing absent some other injury.” *Amalgamated Clothing and Textile Workers Union, AFL-CIO, CLC v. BRLR, Inc.*, No. 2:91-cv-00607, 1993 WL 561879, at *3 (M.D.N.C. Nov. 19, 1993); *see Simon v. E. Ky. Welfare Rights Org.*, 426 U.S. 26, 40 (1976) (“[A]n organization’s abstract concern with a subject that could be affected by an adjudication does not substitute for the concrete injury required by Art. III”). Plaintiff thus does not sufficiently allege an injury-in-fact, a causal link between Defendants’ alleged conduct and any injury, and redressability, and Plaintiff lacks organizational standing.⁹

B. BECAUSE PLAINTIFF DOES NOT ALLEGE THAT THE PATIENTS, TAXPAYERS, AND CONSUMERS IT PURPORTS TO “REPRESENT” CONTROL KEI’S FUNCTIONS, ELECT OR SERVE ON KEI’S LEADERSHIP, OR FINANCE KEI’S ACTIVITIES, PLAINTIFF LACKS ASSOCIATIONAL STANDING

“Since they allege no injury to themsel[f] as [an] organization[] ... [Plaintiff] can establish standing only as representatives of those of their members who have been injured in fact, and thus

⁸ Such taxpayers themselves would lack standing. *See, e.g., Cobb v. U.S. Dep’t of Educ. Office for Civil Rights*, No. 05-2439, 2006 WL 1662965, at *7 (D. Minn. June 15, 2006) (“There is a well-established rule barring federal taxpayer standing.”).

⁹ Although KEI may incur litigation and other expenses in bringing this suit, “[a]n organization cannot, of course, manufacture the injury necessary to maintain a suit from its expenditure of resources on that very suit.” *Spann v. Colonial Village, Inc.*, 899 F.2d 24, 27 (D.C. Cir. 1990).

could have brought suit in their own right.” *Simon*, 426 U.S. at 40. Stated differently, because Plaintiff lacks organizational standing, the analysis turns on whether Plaintiff has sufficiently pled facts to support associational standing.

The caselaw is established that

an association has standing to assert the rights of its members if: (1) the association’s members would have standing to sue in their own right, (2) the interests the association seeks to protect are “germane to the organization’s purpose,” and (3) the claim asserted and the relief requested do not require the participation of individual members in the lawsuit.

Fielder, 435 F. Supp. 2d at 486 (quoting *Hunt v. Wash. State Apple Advertising Comm’n*, 432 U.S. 333, 343 (1977)). Plaintiff does not allege that it has “members”; instead it contends it maintains “multiple email lists,” one of which allegedly has “approximately 2400 subscribers,” and abstractly alleges that it “represents” “patients, taxpayers and consumers” Complaint ¶ 14. Thus, Plaintiff cannot satisfy the above-referenced associational-standing factors, given that it apparently has no members.

But “an organization with no formal members can still have associational standing if it is the functional equivalent of a traditional membership organization.” *Wash. Legal Found. v. Leavitt*, 477 F. Supp. 2d 202, 208 (D.D.C. 2007) (internal citations and quotation marks omitted). The caselaw has developed a “functional equivalency” test, under which an organization may have associational standing – despite a lack of membership – “if the organization (1) serves a specialized segment of the community; (2) represents individuals that have all the indicia of membership, including (i) electing the entity’s leadership, (ii) serving in the entity, and (iii) financing the entity’s activities, and (3) its fortunes are tied closely to those of its constituency.” *Heap v. Carter*, 112 F. Supp. 3d 402, 418 (E.D. Va. 2015).

Plaintiff fails the “indicia-of-membership” test. There is nothing in the Complaint tending to show that any of the “patients, taxpayers and consumers” Plaintiff purports to “represent,” *see* Complaint ¶ 14, (i) elects KEI’s leadership (or even of what KEI’s leadership is comprised), (ii) serves in KEI’s activities and goings-on (whatever they may be), or (iii) finances KEI’s budget.¹⁰ Although there is a wide-body of caselaw applying the above-cited indicia-of-membership test – with many cases granting associational standing, with many others declining to grant associational standing – this is not a case in which a detailed analysis, analogizing and distinguishing that caselaw, is warranted. Simply put, there is nothing in the Complaint from which the Court could conclude that KEI has satisfied the indicia-of-membership test, and thus conclude that KEI has associational standing. *See, e.g., Heap*, 112 F. Supp. 3d at 418-19 (holding that a non-profit organization lacked associational standing where it “provided no details about who the membership is or whether [it] can be considered a voluntary membership organization or a functional equivalent,” and, as such, “[t]his makes it difficult to determine whether it is, in fact, an organization capable of asserting associational standing or whether one of its members has standing to assert the claims at issue,” because the organization “has not alleged any information that would allow the Court to find that it has the kind of leadership and financial structure that is closely tied to that of its members or that its members exert any control over the direction of the organization”).¹¹

¹⁰ Plaintiff does not allege that the patients, taxpayers, and consumers it purports to “represent” pay dues of any sort.

¹¹ The only connection of which the Complaint speaks between KEI and those it “represents” are KEI’s “multiple email lists,” one of which has “approximately 2400 subscribers.” *See* Complaint ¶ 5. But Plaintiff does not identify such subscribers (or allege whether Plaintiff knows their identities) or allege that they are the patients, taxpayers, and consumers Plaintiff purports to represent. In any event, merely having mailing or email lists to which people subscribe is

Absent from the Complaint are any allegations relating to certain “key factors” the cases have identified tending to bear on the indicia-of-membership test. *See Advocates for Am. Disabled Individuals LLC v. Price Co.*, No. 2:16-cv-02141, 2016 WL 5939467, at *3 (D. Ariz. Oct. 13, 2016). These include:

- **Control.** *See Heap*, 112 F. Supp. 3d at 419 (denying associational standing where plaintiff did not allege that “its members exert any control over the direction of the organization”); *Basel Action Network v. Maritime Admin.*, 370 F. Supp. 2d 57, 70 (D.D.C. 2005) (denying associational standing where there was no evidence that the purported members “have any control over the direction or organization of the [plaintiff]”); *Grp. Health Plan, Inc. v. Philip Morris, Inc.*, 86 F. Supp. 2d 912, 918 (D. Minn. 2000) (“In order to meet this ‘indicia of membership’ test, the constituents of an organization must exercise a certain measure of control over the organization.”); *Health Research Group v. Kennedy*, 82 F.R.D. 21, 26 (D.D.C. 1979) (“Absent this element of control, there is simply no assurance that the party seeking judicial review represents that injured Party, and not merely a well-informed point of view”).
- **Electing and Serving on Leadership.** *See Leavitt*, 477 F. Supp. 2d at 208 (denying associational standing where plaintiff’s “supporters [did not] play any role in selecting ... leadership”) (citing *Am. Legal Found. v. FCC*, 808 F.2d 84, 90 (D.C. Cir. 1987)); *Gettman v. DEA*, 290 F.3d 430, 435 (D.C. Cir. 2002) (denying associational standing where plaintiffs “have not shown that its readers and subscribers played any role in selecting its leadership”) (internal quotation marks omitted); *Carespring Healthcare Mgmt., LLC v. Dungey*, No. 1:16-cv-01051, 2018 WL 1138428, at *9 (S.D. Ohio Mar. 2, 2018) (denying associational standing where “there is no allegation that the residents of the Plaintiff nursing homes have any say as to the leadership at the homes”); *Mental Hygiene Legal Serv. v. Cuomo*, 13 F. Supp. 3d 289, 295-96 (S.D.N.Y. 2014), *aff’d*, 609 F. App’x 693 (2d Cir. 2015) (explaining that “if an organization has an active client base and is led by an inclusive leadership, it has sufficient indicia of membership to show that it functions effectively as a membership organization for the purposes of associational standing,” and holding that plaintiff lacked standing where it “concede[d] that its constituents do not elect [or] serve ... the agency’s activities”); *Conservative Baptist Ass’n of Am., Inc. v. Shinseki*, 42 F. Supp. 3d 125, 133 (D.D.C. 2014) (“To determine whether an individual is a member of an organization, the Court looks to whether that individual possesses the ‘indicia’ of membership, which include electing the leadership of the association”).
- **Financing Group’s Activities.** *See Am. Legal Found.*, 808 F.2d at 90 (denying associational standing where plaintiff’s “have not shown that its readers and subscribers played any role in ... financing [its] activities”); *Cuomo*, 609 F. App’x at 695 (affirming district court’s denial of associational standing where plaintiff’s constituents “do not finance its activities”)

insufficient to pass the indicia-of-membership test. *See, e.g., Wash. Legal Found. v. Leavitt*, 477 F. Supp. 2d, 202, 210 (D.D.C. 2007) (rejecting the contention that a person is a “member” if he or she “request[ed] to be placed on one or more of [the organization]’s mailing lists”).

(internal quotation marks omitted); *Price Co.*, 2016 WL 5939467, at *3 (“Key factors include whether … the proposed constituency financed the association’s activities”); *Leavitt*, 477 F. Supp. 2d at 209 (denying associational standing where plaintiff “has not indicated that [its purported members] financially support [it]”).

Plaintiff merely repeats its allegation that it “represents” patients, taxpayers, and consumers. *See* Complaint ¶¶ 5, 14, 24, 69. This falls well short of what the courts have held to be a sufficient pleading of the indicia-of-membership test. Because the Complaint lacks facts tending to show that the patients, taxpayers, and consumers Plaintiff purports to “represent” control KEI’s functions, elect or serve on KEI’s leadership, and finance KEI’s activities, Plaintiff lacks associational standing.

V. CONCLUSION

KEI is a public-interest organization that apparently often opines on the costs of new medical technologies. That Defendant challenges its Article III standing to bring this suit “is not to say that Plaintiffs are insufficiently interested in the subject or even unqualified to debate these issues.” *Philip Morris, Inc.*, 86 F. Supp. 2d at 918. But a “‘mere interest in a problem,’ no matter how longstanding the interest and no matter how qualified the organization is in evaluating the problem, is not sufficient by itself to [confer standing].” *Id.* (quoting *Sierra Club v. Morton*, 405 U.S. 727, 739 (1972)). As explained above, because Plaintiff lacks both organizational and associational standing, the Court should dismiss the Complaint for lack of subject-matter jurisdiction, under Rule 12(b)(1).

Respectfully submitted,

Robert K. Hur
United States Attorney

By: /s/
Alan C. Lazerow (Bar No. 29756)
Assistant United States Attorney
36 S. Charles St., 4th Floor
Baltimore, Maryland 21201
(410) 209-4800
Alan.Lazerow@usdoj.gov

From: Fine, Amanda (NIH/OD) [E] [/O=NIH/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=FINEAB]
Sent: 10/24/2016 7:10:44 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=OD/cn=ROHRBAUM]; McBurney, Margaret (NIH/OD) [E] [/O=NIH/OU=Nihexchange/cn=cc/cn=mmcburney]; Hardesty, Rebecca (NIH/OD) [C] [/O=NIH/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=Hardestyrs2ae]
CC: Myles, Renate (NIH/OD) [E] [/O=NIH/OU=Nihexchange/cn=recipients/cn=mylesr]; Wojtowicz, Emma (NIH/OD) [E] [/O=NIH/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=Wojtowiczeme6d]
Subject: FW: Interview request/chlorcyclizine pricing: BuzzFeed News
Attachments: Reasonable Pricing - Virotas NIH .pdf

Greetings-

I'm including all three of you per Mark's out of office and given that the reporter's deadline is October 28.

NIDDK received the below inquiry from Dan Vergano at Buzzfeed regarding Knowledge Ecology International's (KEI) questions about the drug chlorcyclizine which had/has a small trial at the CC. Attached is a back and forth with NIDDK/NCATS that KEI got through FOIA. Dan's questions are below. In the past when we discuss drug pricing we've used some standard language below and included something specific about the drug in question. Would you be able to help us draft a response to Dan's questions?

b5

Thank you in advance for your input and guidance,
Amanda

Amanda Fine
Deputy, News Media Branch
National Institutes of Health
Tel: 301-496-7246
Email: amanda.fine@nih.gov
Web: <http://www.nih.gov>

NIH . . . Turning Discovery Into Health

From: Payne, January (NIH/NIDDK) [E]
Sent: Monday, October 24, 2016 2:54 PM
To: OCPLPressTeam <OCPLPressTeam@od.nih.gov>; ODOCPL Interviews (NIH/OD OCPL) <ODOCPLInterviews@mail.nih.gov>
Cc: NIDDK NIDDKMEDIA (NIH/NIDDK) <niddkmedia@niddk.nih.gov>
Subject: Interview request/chlorcyclizine pricing: BuzzFeed News

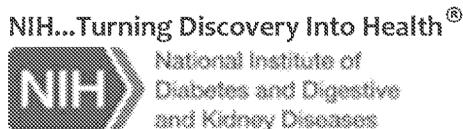
Hello, NIDDK received an interview request from a Buzzfeed reporter asking about NIH involvement in licensing and drug pricing for chlorcyclizine. Chuck Niebylski, director of NIDDK's Technology Advancement Office, asked that I refer this request to NIH OD as it involves NIH's policy on drug pricing.

REL0000024401

Below is the complete email exchange I've had with the reporter, Dan Vergano, and attached is a PDF of an email chain between NIH employees that the reporter received via a public interest group called [Knowledge Ecology International](#), which obtained the records via a FOIA request. (Please note, for background: KEI also [published this 2015 post](#) about the same drug.)

Is NIH OD able to respond to this request?

Thank you,
January W. Payne
Office of Communications and Public Liaison
National Institute of Diabetes and Digestive and Kidney Diseases
NATIONAL INSTITUTES OF HEALTH
Direct 301-435-8115
Cell **b6**
Office 301-496-3583
www.niddk.nih.gov



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From: Dan Vergano [<mailto:dan.vergano@buzzfeed.com>]
Sent: Monday, October 24, 2016 12:29 PM
To: Payne, January (NIH/NIDDK) [E] <january.payne@nih.gov>
Subject: Re: BuzzFeed News: press contact / licensing

January,

Thanks for getting back to me

-- The drug is chlorcyclizine (link to license ann't below), and the public interest group, Knowledge Ecology International (which often looks at NIH licenses) is complaining that its request for "reasonable pricing" requirements in the license were brushed aside to the detriment of taxpayers. The group has just received a public records request (a portion is attached) and suggests they show that NIH is worried more about scaring off the licensee than benefiting the taxpayers who funded this drug and have no assurance they won't have to pay excessively high prices for it.

-- I'm looking for an agency response to this contention.

-- My deadline is 10/28/16 at 5 PM EDT

-- My questions would basically be:

How do you respond to their complaint?

What are the institute's priorities when licensing these drugs?

How much progress has this licensee made on marketing this drug?

What were the results of the Phase 1 trial that NIH funded on this drug?

Some observers are asking: why grant an exclusive license to a small, unknown company with no track record of bringing drugs to market?

I'd have follow-ups depending on the answers, natch, and would want to hear any responses to smarter questions on all this that your folks might have.

Any help appreciated,

Dan Vergano
BuzzFeed News

REL0000024401

b6

Dan Vergano | Science Reporter (DC) | b6
BuzzFeed
1630 Connecticut Ave. 7th Floor, Washington DC 20009

link: <https://s3.amazonaws.com/public-inspection.federalregister.gov/2015-06974.pdf>

Dan Vergano | Science Reporter (DC) | b6
BuzzFeed
1630 Connecticut Ave. 7th Floor, Washington DC 20009

On Mon, Oct 24, 2016 at 11:57 AM, Payne, January (NIH/NIDDK) [E] <january.payne@nih.gov> wrote:

Dear Dan,

Thanks for your message. Can you please provide more information so I can look into your request?

- What is the drug name, and can you please briefly describe the issue that has been raised? Also, what is the name of the public interest group?
- What is your hard deadline?
- Can you please provide a few examples of questions you'd like to ask?

Best,

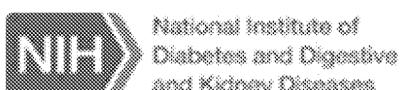
January W. Payne

Office of Communications and Public Liaison
National Institute of Diabetes and Digestive and Kidney Diseases

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REL0000024401

From: Dan Vergano [mailto:dan.vergano@buzzfeed.com]
Sent: Monday, October 24, 2016 11:25 AM
To: NIDDK NIDDKMEDIA (NIH/NIDDK) <niddkmedia@niddk.nih.gov>
Subject: Fwd: BuzzFeed News: press contact / licensing

Krysten's email responder suggested I send this note to this contact. I have also left a phone message with the press office. I am looking for comment this week.

Ms. Carrera,

I'm a science reporter at BuzzFeed News. I'm looking for a press contact at NIDDK who can address a drug licensing issue at your institute. A public interest group is raising questions about one of your licenses and I'd like to get a response from the institute.

Thanks for any help,

Dan Vergano

BuzzFeed News

b6

Dan Vergano | Science Reporter (DC)
BuzzFeed
1630 Connecticut Ave. 7th Floor, Washington DC 20009

JANUARY PAYNE

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[National Institutes of Health | 9000 Rockville Pike, Bethesda, MD 20892, USA](#) | Official website of the National Institutes of Health (NIH). NIH is one of the world's foremost medical research centers. An agency of...



[January Payne on LinkedIn](#)



[@NIH | 663K followers | 6K tweets](#) - 3 hours ago

There's still time to submit your [@NIH_LRP](#) application! Get started on yours today. Deadline is Nov.15 bit.ly/2e7QDzt #studentdebt



[Search for January Payne on Google](#)

Dan is using Senders. [View / edit](#) your own Card

From: Portilla, Lili (NIH/NCATS) [E]
Sent: 29 Apr 2015 11:40:36 -0400
To: McConnell, Cindy (NIH/NCATS) [E]; Niebylski, Charles (NIH/NIDDK) [E]
Subject: RE: ACTION: KEI questions

I agree with chuck and question on NIH involvement on pricing needs to be directed to Bldg 1. Pricing is not in NIH's sphere of influence.

*Lili M. Portilla, MPA
Director, Strategic Alliances
National Center for Advancing Translational Sciences (NCATS), NIH
P: 301-217-2389
E: LiliP@nih.gov*

From: McConnell, Cindy (NIH/NCATS) [E]
Sent: Wednesday, April 29, 2015 11:36 AM
To: Niebylski, Charles (NIH/NCATS) [E]; Portilla, Lili (NIH/NCATS) [E]
Subject: RE: ACTION: KEI questions

Thanks, Chuck!

From: Niebylski, Charles (NIH/NCATS) [E]
Sent: Wednesday, April 29, 2015 11:31 AM
To: McConnell, Cindy (NIH/NCATS) [E]; Portilla, Lili (NIH/NCATS) [E]
Subject: RE: ACTION: KEI questions

IMO, I think the pricing issue is a policy question to be addressed by Dorit or Bldg 1.

The issue about company name is an OTT question.
The company's name was publicly disclosed in the Fed Register Notice: "Virotas Biopharmaceuticals, LLC, a company having a place of business in California".
However, I'm guessing all additional info about the company might be considered business confidential, but OTT needs to opine.
In general, public records of all companies are publicly available from the state where they are incorporated. KEI should ask this question of California or Delaware, or wherever Virotas is incorporated.

From: McConnell, Cindy (NIH/NCATS) [E]
Sent: Wednesday, April 29, 2015 10:41 AM
To: Niebylski, Charles (NIH/NCATS) [E]; Portilla, Lili (NIH/NCATS) [E]
Subject: RE: ACTION: KEI questions

Hi Chuck and Lili,

Please see Mary's notes below. Do you know the answers to her questions? Re the first one, that's not NIH's role/authority; how could we possibly "protect against price gouging"? I'm not sure how to answer her second question, but I'm not convinced it's relevant in this situation (?)

Best,
Cindy

From: Harris, Mary (NIH/NIDDK) [E]
Sent: Wednesday, April 29, 2015 9:13 AM
To: McConnell, Cindy (NIH/NCATS) [E]
Cc: Carrera, Krysten (NIH/NIDDK) [E]
Subject: Re: ACTION: KEI questions

Chuck makes good points. It also doesn't hurt to document and describe the process of bringing drug to market and NIH's place in that process. And does NIH do anything to help protect against price gouging when we invest public funds in development?

We also run the risk of appearing to be hiding something by ignoring KEI's request for information about the company. If we have requested info on the company is it protected under the privacy act?

On Apr 29, 2015, at 8:08 AM, McConnell, Cindy (NIH/NCATS) [E] <mcconnellc@mail.nih.gov> wrote:

Good morning, Mary and Krysten.

I shared Anna's note with Chuck Niebylski and Lili Portilla yesterday, and in turn wanted to share Chuck's response, below, with you.

Best,
Cindy

From: Niebylski, Charles (NIH/NCATS) [E]
Sent: Tuesday, April 28, 2015 8:26 PM
To: McConnell, Cindy (NIH/NCATS) [E]
Cc: Portilla, Lili (NIH/NCATS) [E]
Subject: Re: ACTION: KEI questions

Everything Anna says is true, including that we need industry to bring the fruit of our labors to market. I think KEI will agree too. But KEI's point will be that is precisely why they submitted their letter: they just want to make sure the license transaction between publicly funded research and profit making industry is such that there is no perceived price gouging. This seems like a slippery slope if we simply say we (public researchers) need industry... KEI is ready to serve in that role as liaison for pricing policy. To really address this we would have to make an NIH policy statement on drug pricing, and I think [REDACTED] (b) (5)

(b) (5)

(b) (5)

[REDACTED] As a teachable moment, the next best thing might be to note some other players in the bench to bedside ecosystem (eg FDA etc) and imply that NIH is largely at the bench end of things.

Sent from my iPhone

On Apr 28, 2015, at 7:16 PM, "McConnell, Cindy (NIH/NCATS) [E]" <mcconnelle@mail.nih.gov> wrote:

Just an FYI at this point:

From: Amar, Anna (NIH/NIDDK) [E]
Sent: Tuesday, April 28, 2015 6:50 PM
To: Chang, Kevin (NIH/OD) [E]
Cc: Carrera, Krysten (NIH/NIDDK) [E]; Harris, Mary (NIH/NIDDK) [E]; McConnell, Cindy (NIH/NCATS) [E]
Subject: Re: ACTION: KEI questions

Is there other language that the company would be comfortable with that we could use to clarify for KEI that NIH can not bring the fruits of our research to the public as an FDA approved product without partnering with industry? I'm not sure KEI understands the new compound requires a lot more investment before it can be used in patients.

Also, do we have to identify the company at this time? It would be unfortunate if KEI, in their understandable excitement to have low cost treatments, unwittingly bothers the company enough that they might reconsider the license. [REDACTED] (b) (5)
[REDACTED] (b) (5)

Best,

Anna Z. Amar
Acting Deputy Director
NIDDK Technology Advancement Office
Ph: 301-435-2305
aa54d@mail.nih.gov

On Apr 28, 2015, at 4:36 PM, Chang, Kevin (NIH/OD) [E] <changkc@mail.nih.gov> wrote:

Dear Krysten,

We received back the comments from the company and they are comfortable with the following.

"Virotas Biopharmaceuticals, LLC is a start-up company with founders experienced in drug development and commercialization."

We appreciate the effort that was put forth in your suggested language but are not comfortable stating anything further beyond the statement above.

If you have any questions, please contact me.

Best regards,

Kevin

Kevin W. Chang, Ph.D.
Senior Licensing and Patenting Manager
NIH Office of Technology Transfer
8011 Executive Blvd, Suite 325
Rockville, MD 20852
Phone: (301) 435-5018
Fax: (301) 402-0220

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From: Carrera, Krysten (NIH/NIDDK) [E]
Sent: Monday, April 27, 2015 10:07 AM
To: Chang, Kevin (NIH/OD) [E]
Cc: Harris, Mary (NIH/NIDDK) [E]; McConnell, Cindy (NIH/NCATS) [E]; Amar, Anna (NIH/NIDDK) [E]
Subject: RE: ACTION: KEI questions

Good morning – just touching base about the email below. Is OTT comfortable addressing #4, and having me transmit the answer on your behalf? Thank you.

P/YI, we'll likely add this language, or something very similar, after your answer to #4; please let me know if it looks alright.

(b) (5)

From: Carrera, Krysten (NIH/NIDDK) [E]
Sent: Friday, April 24, 2015 8:22 AM

To: Chang, Kevin (NIH/OD) [E]
Cc: Harris, Mary (NIH/NIDDK) [E]; McConnell, Cindy (NIH/NCATS) [E]; Amer, Anna (NIH/NIDDK) [E]
Subject: ACTION: KEI questions

Hi Kevin,

Please see the questions from KEI below. NIDDK and NCATS investigators will address the first three questions. We'll also include language on the value of partnering with industry to bring treatments to market. The last question, 4, I think OTT would need to handle. I can transmit your answer together with the science-related answers.

Sound okay to you?

Thanks,

Krysten Carrera

Media Relations and Public Liaison Team
National Institute of Diabetes and Digestive and Kidney Diseases
National Institutes of Health
(301) 435-8112
(b) (6)
(c) [REDACTED]
krystencarrera@nidk.nih.gov

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From: [REDACTED] (b) (6) **On Behalf Of** Elizabeth Rajasingh
(mailto:[REDACTED])
Sent: Thursday, April 23, 2015 3:08 PM
To: Carrera, Krysten (NIH/NIDDK) [E]
Subject: Re: questions for our researchers

Hi Krysten,

Yes, I have tried to speak with the authors of that article about their research. I have a few questions regarding their work.

1) Is the compound referenced in the article, "Repurposing of the antihistamine chlorcyclizine and related compounds for treatment of hepatitis C virus infection," the same compound that is referenced in the Federal Register, "Prospective Grant of Exclusive License: Small Molecule Therapeutics Against Hepatitis C Virus Infection?"

- 2) Can you describe the next steps you will be taking to further this research? Does the compound appear to be a cure/game changer? Does it have the potential to be a low-cost form of treatment for Hep C patients?
- 3) Is the NIH still funding research, specifically clinical trials, on this compound? If so, can you provide details on the cost of the clinical trials that the NIH is funding?
- 4) Can you provide any information about the pharmaceutical company that is seek the exclusive license in the previously mentioned federal register notice, such as names, addresses or titles in the company (board of directors or shareholders)?

Thank you for your help,
Elizabeth Rajasingh

Elizabeth Rajasingh
Peris Research and Policy Fellow, Knowledge Ecology International
1621 Connecticut Ave. NW, Suite 500
Washington, DC 20009
elizabeth.rajasingh@keionline.org | 1-202-332-2670

On Thu, Apr 23, 2015 at 9:11 AM, Carrera, Krysten (NIH/NIDDK) [E] <krysten.carrera@nih.gov> wrote:
Dear Ms. Rajasingh,

We understand you have been reaching out to the authors of the recent publication, "Repurposing of the antihistamine chlorcyclizine and related compounds for treatment of hepatitis C virus infection." What specific questions do you have regarding the science? We would be happy to send written responses on behalf of the authors to help them manage their time and focus on their research.

Thanks,

Krysten Carrera
Media Relations and Public Liaison Team

National Institute of Diabetes and Digestive and Kidney Diseases
National Institutes of Health

(f) [REDACTED] (b) (6)

(c) [REDACTED]
krysten.carrera@nih.gov

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<image001.jpg>

<image001.jpg>

<image001.jpg>

From: Liang, Jake (NIH/NIDDK) [E] </O=NIH/OU=NIHEXCHANGE/CN=NIDDK/CN=JAKEL>
To: Carrera, Krysten (NIH/NIDDK) [E] </O=NIH/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOH-F23SPDLT)/CN=RECIPIENTS/CN=Carrera&id>
CC: McConnell, Cindy (NIH/NCATS) [E]
 </O=NIH/OU=NIHEXCHANGE/cn=Recipients/cn=mcconnellc>;
 "Chang, Kevin (NIH/OD) [E] </O=NIH/OU=NIHEXCHANGE/cn=RECIPIENTS/cn=CHANGKE>";
 "Amar, Anna (NIH/NIDDK) [E] </O=NIH/OU=NIHEXCHANGE/cn=niddk/cn=aamar>";
 "Harris, Mary (NIH/NIDDK) [E] </O=NIH/OU=NIHEXCHANGE/cn=NIDDK/cn=HarrisMN>"
Subject: Re: FOR REVIEW: KEI answers
Date: 2015/04/30 19:27:16
Priority: Normal
Type: Note

Made a few edits in answer to question #2.

> On Apr 30, 2015, at 5:09 PM, Carrera, Krysten (NIH/NIDDK) [E] <krysten.carrera@nih.gov> wrote:
>
> Good afternoon,
>
> Please review the answers to the questions Knowledge Ecology International sent, making any edits as
track changes or approving as-is. Please reply-all. The attached document contains contributions and/or
edits from NCATS, NIDDK and OTT. When we all agree on a version, I will transmit the answers to KEI.
>
> Feel free to give me a call to discuss further.
>
> Thank you.
>
> Krysten Carrera
> Media Relations and Public Liaison Team
> National Institute of Diabetes and Digestive and Kidney Diseases
> National Institutes of Health
> (010) 301-435-6112
> (e-mail removed) (b) (6)
> krysten.carrera@nih.gov
> NIH...Turning Discovery Into Health®
>
> <image001.jpg>
> <answersNCATSNIDDK&OTTedits.docx>

Sender: Liang, Jake (NIH/NIDDK) [E] </O=NIH/OU=NIHEXCHANGE/CN=NIDDK/CN=JAKEL>
Recipient: Carrera, Krysten (NIH/NIDDK) [E] </O=NIH/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOH-F23SPDLT)/CN=RECIPIENTS/CN=Carrera&id>
"McConnell, Cindy (NIH/NCATS) [E]
 </O=NIH/OU=NIHEXCHANGE/cn=Recipients/cn=mcconnellc>;
 "Chang, Kevin (NIH/OD) [E] </O=NIH/OU=NIHEXCHANGE/cn=RECIPIENTS/cn=CHANGKE>";
 "Amar, Anna (NIH/NIDDK) [E] </O=NIH/OU=NIHEXCHANGE/cn=niddk/cn=aamar>";
 "Harris, Mary (NIH/NIDDK) [E] </O=NIH/OU=NIHEXCHANGE/cn=NIDDK/cn=HarrisMN>"

Sent Date: 2015/04/30 19:27:07

Delivered Date: 2015/04/30 19:27:16

REL0000024401.0001

From: Carrera, Krysten (NIH/NIDDK) [E]
Sent: 1 May 2015 16:43:37 -0400
To: [REDACTED] (b) (6)
Subject: RE: questions for our researchers

Hi Elizabeth.

Thanks for your patience. Here are our answers to your questions.

Best,
Krysten Carrera

1) Is the compound referenced in the article, "Repurposing of the antihistamine chlorcyclizine and related compounds for treatment of hepatitis C virus infection," the same compound that is referenced in the Federal Register, "Prospective Grant of Exclusive License: Small Molecule Therapeutics Against Hepatitis C Virus Infection?"

The patent applications referenced in the Federal Register cover several new classes of compounds that have the potential of being a new treatment against the hepatitis C virus. One class is related to chlorcyclizine, the antihistamine compound described in the paper. This molecule is an over-the-counter drug that already is in the public domain.

2) Can you describe the next steps you will be taking to further this research? Does the compound appear to be a cure/game changer? Does it have the potential to be a low-cost form of treatment for Hep C patients?

In an FDA-approved clinical trial at the NIH Clinical Center, researchers are testing chlorcyclizine, one of the over-the-counter antihistamines described in the paper. The small study is evaluating the compound's safety and identifying any side effects in people who have hepatitis C, and is also designed to assess whether this compound has any antiviral effect with a short-term dosing. This study will not determine whether this compound can be used to treat the hepatitis C virus. Currently we do not know if the drug has any effect in people infected with the virus. Even if the initial trial raises no serious safety concerns, FDA would require additional, larger clinical trials to further study safety and to determine efficacy of the drug to treat the hepatitis C virus. FDA would consider the results of the clinical trials before deciding if the drug should be approved for use in hepatitis C.

The NIH values partnerships with industry and academia to deliver groundbreaking technology and medical advances to the public as quickly as possible. These collaborations help innovative ideas become reality, leveraging resources and expertise from a variety of disciplines. The NIH contributes scientific knowledge and discoveries from the research it supports and does not control approval or pricing of drugs.

3) Is the NIH still funding research, specifically clinical trials, on this compound? If so, can you provide details on the cost of the clinical trials that the NIH is funding?

The clinical trial is a small phase 1b study supported by the NIH Intramural Research Program. The cost is part of the program's operating budget and does not require additional funding.

4) Can you provide any information about the pharmaceutical company that is seek the exclusive license in the previously mentioned federal register notice, such as names, addresses or titles in the company (board of directors or shareholders)?

Virotas Biopharmaceuticals, LLC is a privately held start-up company with founders experienced in drug development and commercialization.

cid:image001.jpg@01CE68D4.35225140

From: [REDACTED] (b) (6) [mailto:[REDACTED] (b) (6)] On Behalf Of Elizabeth Rajasingh
Sent: Thursday, April 23, 2015 3:08 PM
To: Carrera, Krysten (NIH/NIDDK) [E]
Subject: Re: questions for our researchers

Hi Krysten,

Yes, I have tried to speak with the authors of that article about their research. I have a few questions regarding their work.

- 1) Is the compound referenced in the article, "Repurposing of the antihistamine chlorcyclizine and related compounds for treatment of hepatitis C virus infection," the same compound that is referenced in the Federal Register, "Prospective Grant of Exclusive License: Small Molecule Therapeutics Against Hepatitis C Virus Infection?"
- 2) Can you describe the next steps you will be taking to further this research? Does the compound appear to be a cure/game changer? Does it have the potential to be a low-cost form of treatment for Hep C patients?
- 3) Is the NIH still funding research, specifically clinical trials, on this compound? If so, can you provide details on the cost of the clinical trials that the NIH is funding?
- 4) Can you provide any information about the pharmaceutical company that is seek the exclusive license in the previously mentioned federal register notice, such as names, addresses or titles in the company (board of directors or shareholders)?

Thank you for your help,
Elizabeth Rajasingh

Elizabeth Rajasingh
Peris Research and Policy Fellow, Knowledge Ecology International
1621 Connecticut Ave. NW, Suite 500
Washington, DC 20009
elizabeth.rajasinhg@keionline.org | 1-202-332-2670

On Thu, Apr 23, 2015 at 9:11 AM, Carrera, Krysten (NIH/NIDDK) [E] <krysten.carrera@nih.gov> wrote:
Dear Ms. Rajasingh,

We understand you have been reaching out to the authors of the recent publication, "Repurposing of the antihistamine chlorcyclizine and related compounds for treatment of hepatitis C virus infection." What specific questions do you have regarding the science? We would be happy to send written responses on behalf of the authors to help them manage their time and focus on their research.

Thanks,

Krysten Carrera

Media Relations and Public Liaison Team
National Institute of Diabetes and Digestive and Kidney Diseases
National Institutes of Health
(t) 301-435-8112
(c) [REDACTED] (b) (6)
krysten.carrera@nih.gov

NIH...Turning Discovery Into Health®

[REDACTED]
cid:image001.jpg@01CE68D4.35225140

Sender: Carrera, Krysten (NIH/NIDDK) [/O=NIH/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=CARRERAKD]<
Recipients: "Chang, Kevin (NIH/QD) [/O=NIH/OU=NIHEXCHANGE/cn=RECIPIENTS/cn=CHANGKE]<;
"Harris, Mary (NIH/NIDDK) [/O=NIH/OU=NIHEXCHANGE/cn=NIDDK/cn=HarrisMN]>";
"McConnell, Cindy (NIH/NCATS) [/O=NCI/OU=NIHEXCHANGE/cn=Recipients/cn=mcconnellc]>";
"Amar, Anna (NIH/NIDDK) [/O=NIH/OU=NIHEXCHANGE/cn=nlaid/cn=aamar]>"

Sent Date: 2015/04/27 10:07:02

Delivered Date: 2015/04/27 10:07:03

From: Columbus, Megan (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=E8878F99917841749C5AE3FAD8D90C73-COLUMBUM]
Sent: 3/22/2018 2:13:44 PM
To: Bayha, Ryan (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=5d5a4353cd514322a8598dbb1751ee79-bayhar]; Wojtowicz, Emma (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=45c6610aca6e44a08d497630425e5ecd-wojtowiczem]; Hammersla, Ann (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=87fb28aa23744c0b855ef0683ac2e8b4-hammerslaa]; Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718ccb29fab-rohrbaum]; Jorgenson, Lyric (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=3bbde7d361374981a4d336b6eeb17521-jorgensonla]
CC: Bulls, Michelle G. (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=b366f1a4382d44c1bde626e7730c3dd4-bullsmg]; Jackson, Stephanie (NIH/OD) [C] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=813a0dc9ddbc4fa2be8ca6ea23d081ca-jacksonsg]; Myles, Renate (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=7d317f5626934585b3692a1823c1b522-mylesr]; Fine, Amanda (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=61290b74aa9a44358954c45439ffdeb6-fineab]; Kosub, David (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=3e3eccf57f4e4fcfaecaa7885f39bee5-kosubd]
Subject: RE: question from a journalist

Hi Emma, we should stick with the reference to NIH. Multiple offices may be involved in the determination.

Megan

From: Bayha, Ryan (NIH/OD) [E]
Sent: Thursday, March 22, 2018 9:16 AM
To: Wojtowicz, Emma (NIH/OD) [E] <emma.wojtowicz@nih.gov>; Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>; Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>; Jorgenson, Lyric (NIH/OD) [E] <lyric.jorgenson@nih.gov>
Cc: Bulls, Michelle G. (NIH/OD) [E] <michelle.bulls@nih.gov>; Jackson, Stephanie (NIH/OD) [C] <stephanie.jackson3@nih.gov>; Myles, Renate (NIH/OD) [E] <mylesr@mail.nih.gov>; Fine, Amanda (NIH/OD) [E] <amanda.fine@nih.gov>; Columbus, Megan (NIH/OD) [E] <columbum@od.nih.gov>; Kosub, David (NIH/OD) [E] <david.kosub@nih.gov>
Subject: RE: question from a journalist

+ Lyric for awareness

From: Wojtowicz, Emma (NIH/OD) [E]
Sent: Thursday, March 22, 2018 9:07 AM
To: Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>; Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Cc: Bulls, Michelle G. (NIH/OD) [E] <michelle.bulls@nih.gov>; Jackson, Stephanie (NIH/OD) [C] <stephanie.jackson3@nih.gov>; Myles, Renate (NIH/OD) [E] <mylesr@mail.nih.gov>; Fine, Amanda (NIH/OD) [E] <amanda.fine@nih.gov>; Columbus, Megan (NIH/OD) [E] <columbum@od.nih.gov>; Kosub, David (NIH/OD) [E] <david.kosub@nih.gov>; Bayha, Ryan (NIH/OD) [E] <bayhar@od.nih.gov>
Subject: RE: question from a journalist

Thanks, Ann. I am looping in Megan, David, and Ryan for review and awareness. We are anticipating that reporter may follow up and ask what office reviews and takes action. Is it okay to specify OER? Please see addition in red below. Thanks!

b5

From: Hammersla, Ann (NIH/OD) [E]
Sent: Thursday, March 22, 2018 8:58 AM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>; Wojtowicz, Emma (NIH/OD) [E] <emma.wojtowicz@nih.gov>
Cc: Bulls, Michelle G. (NIH/OD) [E] <michelle.bulls@nih.gov>; Jackson, Stephanie (NIH/OD) [C] <stephanie.jackson3@nih.gov>; Myles, Renate (NIH/OD) [E] <mylesr@mail.nih.gov>; Fine, Amanda (NIH/OD) [E] <amanda.fine@nih.gov>
Subject: RE: question from a journalist

OER working with OSP. Ann

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Wednesday, March 21, 2018 7:48 PM
To: Wojtowicz, Emma (NIH/OD) [E] <emma.wojtowicz@nih.gov>
Cc: Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>; Bulls, Michelle G. (NIH/OD) [E] <michelle.bulls@nih.gov>; Jackson, Stephanie (NIH/OD) [C] <stephanie.jackson3@nih.gov>; Myles, Renate (NIH/OD) [E] <mylesr@mail.nih.gov>; Fine, Amanda (NIH/OD) [E] <amanda.fine@nih.gov>
Subject: Re: question from a journalist

Not OTT

Sent from my iPhone

On Mar 21, 2018, at 5:02 PM, Wojtowicz, Emma (NIH/OD) [E] <emma.wojtowicz@nih.gov> wrote:

Hi Ann-

Quick question, what NIH office would be response for reviewing NIH's support? Is it OTT, or would OER and/or OMA get involved?

Thank you-
Emma

From: Wojtowicz, Emma (NIH/OD) [E]
Sent: Wednesday, March 21, 2018 2:29 PM
To: Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>; Bulls, Michelle G. (NIH/OD) [E] <michelle.bulls@nih.gov>; Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>
Cc: Jackson, Stephanie (NIH/OD) [C] <stephanie.jackson3@nih.gov>; Myles, Renate (NIH/OD) [E] <mylesr@mail.nih.gov>; Fine, Amanda (NIH/OD) [E] <amanda.fine@nih.gov>
Subject: RE: question from a journalist

Thanks, Ann!

From: Hammersla, Ann (NIH/OD) [E]
Sent: Wednesday, March 21, 2018 2:28 PM
To: Wojtowicz, Emma (NIH/OD) [E] <emma.wojtowicz@nih.gov>; Bulls, Michelle G. (NIH/OD) [E] <michelle.bulls@nih.gov>; Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Cc: Jackson, Stephanie (NIH/OD) [C] <stephanie.jackson3@nih.gov>; Myles, Renate (NIH/OD) [E] <mylesr@mail.nih.gov>; Fine, Amanda (NIH/OD) [E] <amanda.fine@nih.gov>
Subject: RE: question from a journalist

All: OER's statement is:

b5

Ann

From: Wojtowicz, Emma (NIH/OD) [E]
Sent: Wednesday, March 21, 2018 12:58 PM
To: Bulls, Michelle G. (NIH/OD) [E] <michelle.bulls@nih.gov>; Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>; Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Cc: Jackson, Stephanie (NIH/OD) [C] <stephanie.jackson3@nih.gov>; Myles, Renate (NIH/OD) [E] <mylesr@mail.nih.gov>; Fine, Amanda (NIH/OD) [E] <amanda.fine@nih.gov>
Subject: RE: question from a journalist

Thanks, Michelle. I will wait for the updated statement from Ann.

From: Bulls, Michelle G. (NIH/OD) [E]
Sent: Wednesday, March 21, 2018 12:57 PM
To: Wojtowicz, Emma (NIH/OD) [E] <emma.wojtowicz@nih.gov>; Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>; Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Cc: Jackson, Stephanie (NIH/OD) [C] <stephanie.jackson3@nih.gov>; Bulls, Michelle G. (NIH/OD) [E] <michelle.bulls@nih.gov>
Subject: RE: question from a journalist

Hi Emma,

Ann will be revising the OER/OPERA statement to add a sentence. Hold tight until she sends it to you.
Please note—the revised statement that you will receive has been approved by Mike Lauer OER DDER.

Thanks!

From: Wojtowicz, Emma (NIH/OD) [E]
Sent: Wednesday, March 21, 2018 11:29 AM
To: Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>; Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>
Cc: Bulls, Michelle G. (NIH/OD) [E] <michelle.bulls@nih.gov>; Jackson, Stephanie (NIH/OD) [C] <stephanie.jackson3@nih.gov>
Subject: RE: question from a journalist

Thanks, Ann

b5

From: Hammersla, Ann (NIH/OD) [E]
Sent: Wednesday, March 21, 2018 11:26 AM
To: Wojtowicz, Emma (NIH/OD) [E] <emma.wojtowicz@nih.gov>; Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Cc: Bulls, Michelle G. (NIH/OD) [E] <michelle.bulls@nih.gov>; Jackson, Stephanie (NIH/OD) [C] <stephanie.jackson3@nih.gov>
Subject: FW: question from a journalist

Dear Emma:

The following is the response approved by OPERA.

b5

Ann

From: Wojtowicz, Emma (NIH/OD) [E]
Sent: Tuesday, March 20, 2018 4:24 PM
To: Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>; Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Cc: Myles, Renate (NIH/OD) [E] <mylesr@mail.nih.gov>; Fine, Amanda (NIH/OD) [E] <amanda.fine@nih.gov>
Subject: RE: question from a journalist

Hi Ann-

I am following up on your email below. Do you have the two-sentence response?

Thanks again for your help!
Emma

From: Hammersla, Ann (NIH/OD) [E]
Sent: Tuesday, March 20, 2018 11:36 AM
To: Wojtowicz, Emma (NIH/OD) [E] <emma.wojtowicz@nih.gov>; Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Cc: Myles, Renate (NIH/OD) [E] <mylesr@mail.nih.gov>; Fine, Amanda (NIH/OD) [E] <amanda.fine@nih.gov>
Subject: RE: question from a journalist

All:

I drafted a 2-sentence this morning and when I receive an OK to send I will. My draft response included

b5

Ann

From: Wojtowicz, Emma (NIH/OD) [E]
Sent: Tuesday, March 20, 2018 11:32 AM
To: Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>
Cc: Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>; Myles, Renate (NIH/OD) [E] <mylesr@mail.nih.gov>; Fine, Amanda (NIH/OD) [E] <amanda.fine@nih.gov>
Subject: RE: question from a journalist

Thanks, Mark. Ann, do you have any input? Thanks!

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Tuesday, March 20, 2018 10:20 AM
To: Wojtowicz, Emma (NIH/OD) [E] <emma.wojtowicz@nih.gov>
Cc: Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>; Myles, Renate (NIH/OD) [E] <mylesr@mail.nih.gov>; Fine, Amanda (NIH/OD) [E] <amanda.fine@nih.gov>
Subject: Re: question from a journalist

Unless you have heard otherwise from Ann, I suggest the previous responses you have used

Sent from my iPhone

On Mar 20, 2018, at 8:46 AM, Wojtowicz, Emma (NIH/OD) [E] <emma.wojtowicz@nih.gov> wrote:

My apologies, I should have specified that Ed's deadline is 10am. Thanks-

From: Wojtowicz, Emma (NIH/OD) [E]
Sent: Tuesday, March 20, 2018 8:31 AM
To: Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>; Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>
Cc: Myles, Renate (NIH/OD) [E] <mylesr@mail.nih.gov>; Fine, Amanda (NIH/OD) [E] <amanda.fine@nih.gov>
Subject: FW: question from a journalist

Hi Mark and Ann

We received an inquiry from Ed Silverman with STAT regarding UPenn transferring patent rights to Aegerion Pharmaceuticals without disclosing that they had received NIH funding, please see the email below. Ed asked a similar question regarding UPenn and CAR T technologies in October. Initially, we provided the following response:

b5

Please advise how we should respond.

Thank you-
Emma

From: Silverman, Ed [<mailto:ed.silverman@statnews.com>]
Sent: Monday, March 19, 2018 5:29 PM
To: Myles, Renate (NIH/OD) [E] <mylesr@mail.nih.gov>; Wojtowicz, Emma (NIH/OD) [E] <emma.wojtowicz@nih.gov>
Subject: question from a journalist

Hi Guys,

An advocacy group, KEI, wrote a letter to Karen Rogers and Jill Roering saying that six patents for a cholesterol treatment held by Aegerion Pharmaceuticals were discovered by a UPenn researcher, but the school - which later transferred the rights to the company - never disclosed NIH grant funding.

The letter is attached and here is a supporting memo...

<https://www.keionline.org/wp-content/uploads/2018/03/Juxtapid-Failure2disclose-Daniel-Rader-19Mar2018.pdf>

KEI says the government has the right to take title and should do so, since failing to disclose the funding violates federal law and regulations.

Wondering what NIH will do. Any comment?

I'm writing about this in the morning.

Thanks
ed silverman
STAT News / Pharmalot
973-493-7851

www.statnews.com/pharmalot/

From: Wong, Jennifer (NIH/NIMH) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=C4258C7CF58F4945A3DF079942C68852-WONGJE]
Sent: 5/17/2019 12:17:08 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718ccb29fab-rohrbaum]
Subject: RE: KEI - Inquiry regarding FR 84 FR 19090 - Prospective Exclusive License on Scopolamine Therapeutics

Sure. I'm available between 11:30 am – 2pm. Is there a specific time that works for you? I can give you a call then.

Thanks,
Jenny

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Thursday, May 16, 2019 5:54 PM
To: Wong, Jennifer (NIH/NIMH) [E] <jennifer.wong2@nih.gov>
Subject: RE: KEI - Inquiry regarding FR 84 FR 19090 - Prospective Exclusive License on Scopolamine Therapeutics

Would sometime tomorrow between 11 and 2 work?

From: Wong, Jennifer (NIH/NIMH) [E] <jennifer.wong2@nih.gov>
Sent: Thursday, May 16, 2019 8:03 AM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Subject: RE: KEI - Inquiry regarding FR 84 FR 19090 - Prospective Exclusive License on Scopolamine Therapeutics

Hi Mark,

Just wondering if you had an opportunity to look at the responses. If it is easier to chat, please let me know.

Thanks!
Jenny

Jennifer Wong, M.S.
Technology Development Coordinator
National Institute of Mental Health
Office of Technology Transfer
35A Convent Drive, Room GE400
Bethesda, MD 20892-3747
Phone: 301-480-4821
E-mail: wongje@mail.nih.gov

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From: Wong, Jennifer (NIH/NIMH) [E]
Sent: Friday, May 10, 2019 1:20 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>
Subject: FW: Inquiry regarding FR 84 FR 19090 - Prospective Exclusive License on Scopolamine Therapeutics

Hi Mark,

Embedded in KEI's email below are draft responses. I wasn't quite sure how to answer some of them - please feel free to make any edits or provide comments/suggestions. Thank you so much!

Best,
Jenny

Jennifer Wong, M.S.
Technology Development Coordinator
National Institute of Mental Health
Office of Technology Transfer
35A Convent Drive, Room GE400
Bethesda, MD 20892-3747
Phone: 301-480-4821
E-mail: wongje@mail.nih.gov

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From: Claire Cassedy <claire.cassedy@keionline.org>
Sent: Friday, May 3, 2019 11:16 AM
To: Wong, Jennifer (NIH/NIMH) [E] <jennifer.wong2@nih.gov>
Cc: James Love <james.love@keionline.org>
Subject: Inquiry regarding FR 84 FR 19090 - Prospective Exclusive License on Scopolamine Therapeutics

Dear Jennifer Wong,

I am writing in reference to the Federal Register notice (FR 84 FR 19090) regarding, "Prospective Grant of Exclusive Patent License: Scopolamine Therapeutics for Depression and Bipolar Disorder," for which you are listed as the contact for inquiries. I was hoping you could provide me with some further information regarding the status of the technologies.

1. At what stage of development are the inventions listed? b5

b5

2. Has the government funded any clinical trials relevant to these technologies? b5

b5

3. If the government has provided funding, how much has been spent by the government on these trials? Can you provide NCT numbers? b5

4. How many years of exclusivity have been offered in this agreement, and what will the royalty rate be? b5

b5

5. Regarding the company to receive the licenses, Repurposed Therapeutics, are any former NIH employees associated with the company? b5

b5

Thank you in advance for your assistance in this matter.

Best Regards,

REL0000024403

Claire Cassedy

--
Claire Cassedy
Knowledge Ecology International
1621 Connecticut Avenue NW
Suite 500
Washington, DC 20009
Tel.: 1.202.332.2670

REL0000024403

From: Berkley, Dale (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=5EE461C29F5045A49F0ADF82CAAA2F31-BERKLEYD]
Sent: 1/11/2019 1:52:56 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718ccb29fab-rohrbaum]
Subject: RE: KEI Response Letter

b5

Dale D. Berkley, Ph.D., J.D.
Office of the General Counsel, PHD, NIH Branch
Bldg. 31, Rm. 47
Bethesda, MD 20892
301-496-6043
301-402-2528(Fax)

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From: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Sent: Thursday, January 10, 2019 5:36 PM
To: Berkley, Dale (NIH/OD) [E] <berkleyd@od.nih.gov>
Subject: FW: KEI Response Letter

b5

From: Soukas, Peter (NIH/NIAID) [E] <peter.soukas@nih.gov>
Sent: Thursday, January 10, 2019 5:23 PM
To: Berkley, Dale (NIH/OD) [E] <berkleyd@od.nih.gov>; Rohrbaugh, Mark (NIH/OD) [E] <crohrbaum@od.nih.gov>
Cc: Puglielli, Maryann (NIH/NIAID) [E] <maryann.puglielli@nih.gov>; Williams, Richard (NIH/NIAID) [E] <rwilliams@niaid.nih.gov>; Frisbie, Suzanne (NIH/NIAID) [E] <suzanne.frisbie@nih.gov>; Mowatt, Michael (NIH/NIAID) [E] <mmowatt@niaid.nih.gov>
Subject: KEI Response Letter

Dear Dale and Mark,

We hope everything is going well with you.

b5

Please contact us if you have any additional questions. Thank you.

Peter Soukas
National Institutes of Health
National Institute of Allergy and Infectious Diseases
Phone: 301-594-8730
Email: ps193c@nih.gov

From: Routh, Jennifer (NIH/NIAID) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=E3B5BBA3619344E38037CA94A71473A8-ROUTHJ]
Sent: 10/17/2017 2:38:51 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718ccb29fab-rohrbaum]; Mowatt, Michael (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=cb1ef7e2e54b4164ae34814574bda638-mmowatt]; Frisbie, Suzanne (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=c402740ceaad4d4f97a8c28f16fbb349-frisbies]
CC: Stover, Kathy (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=c82722674ba14c2f969bd50dfa6a7af4-stoverk]
Subject: RE: For awareness
Attachments: Questions from Ed Silverman at STAT (002) ks.docx

Mark, Mike and Suzanne –

Thanks for your input. We've drafted a response to the reporter (attached) with a few questions in the margin. Please let us know what you think.

Thanks,
Jen

Jennifer Routh [E]
Scientific Communications Editor
Office of Communications and Government Relations
National Institute of Allergy and Infectious Diseases (NIAID)
NIH/HHS
31 Center Drive Room 7A17B
Bethesda, MD 20892
Direct: (301) 496-8327
jennifer.routh@nih.gov

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From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Tuesday, October 17, 2017 10:11 AM
To: Mowatt, Michael (NIH/NIAID) [E] <mmowatt@niaid.nih.gov>; Billet, Courtney (NIH/NIAID) [E] <billetc@niaid.nih.gov>; Fauci, Anthony (NIH/NIAID) [E] <afauci@niaid.nih.gov>
Cc: Mascola, John (NIH/VRC) [E] <jmascola@mail.nih.gov>; Stover, Kathy (NIH/NIAID) [E] <kathy.stover@nih.gov>; Routh, Jennifer (NIH/NIAID) [E] <jennifer.routh@nih.gov>; Conrad, Patricia (NIH/NIAID) [E] <conradpa@niaid.nih.gov>; Folkers, Greg (NIH/NIAID) [E] <gfolkers@niaid.nih.gov>
Subject: RE: For awareness

I agree.

b5

b5

From: Mowatt, Michael (NIH/NIAID) [E]
Sent: Tuesday, October 17, 2017 10:05 AM
To: Billet, Courtney (NIH/NIAID) [E] <billetc@niaid.nih.gov>; Fauci, Anthony (NIH/NIAID) [E] <afauci@niaid.nih.gov>
Cc: Mascola, John (NIH/VRC) [E] <jmascola@mail.nih.gov>; Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>; Stover, Kathy (NIH/NIAID) [E] <kathy.stover@nih.gov>; Routh, Jennifer (NIH/NIAID) [E] <jennifer.routh@nih.gov>; Conrad, Patricia (NIH/NIAID) [E] <conradpa@niaid.nih.gov>; Folkers, Greg (NIH/NIAID) [E] <gfolkers@niaid.nih.gov>;

Mowatt, Michael (NIH/NIAID) [E] <mmowatt@niaid.nih.gov>

Subject: RE: For awareness

Regarding Q2:

b5

Mark may have additional comments.

Mike

From: Billet, Courtney (NIH/NIAID) [E]

Sent: Tuesday, October 17, 2017 9:05 AM

To: Fauci, Anthony (NIH/NIAID) [E] <afauci@niaid.nih.gov>

Cc: Mowatt, Michael (NIH/NIAID) [E] <mmowatt@niaid.nih.gov>; Mascola, John (NIH/VRC) [E] <jmascola@mail.nih.gov>; Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>; Stover, Kathy (NIH/NIAID) [E] <kathy.stover@nih.gov>; Routh, Jennifer (NIH/NIAID) [E] <jennifer.routh@nih.gov>; Conrad, Patricia (NIH/NIAID) [E] <conradpa@niaid.nih.gov>; Folkers, Greg (NIH/NIAID) [E] <gfolkers@niaid.nih.gov>

Subject: For awareness

We have been contacted by STAT's Ed Silverman, author of the piece below from May re Sanofi deal.

We have sent him the Fed Reg notice, and are now working on answers to some follow-up questions, which are (1) why an ***exclusive*** license and (2) assuming we proceed with licensure, will the terms be disclosed. We have the answer to the first question and are seeking the answer to the second. He is not requesting an interview.

<https://www.statnews.com/2017/05/29/zika-vaccine-price/>

US taxpayers are funding a Zika vaccine. Let's make sure US patients can afford it

By ED SILVERMAN
MAY 29, 2017

Dear Acting Secretary Speer,

As you know, the United States must prepare for future outbreaks of the Zika virus, but a high-stakes debate has erupted over a deal the federal government may strike with a private company to develop a vaccine. As acting secretary of the US Army, you have an opportunity — and responsibility — to find a workable solution.

The issue is whether the company — in this case, Sanofi Pasteur — should be required to make the vaccine, which is based on technology discovered with US taxpayer funds, affordable for Americans in return for an exclusive license to develop it into a commercial product.

I understand there are risks, but you should find a way to ensure that Americans do not overpay.

Here's the backstory: Last year, the government gave Sanofi, which is one of the world's largest vaccine makers, a \$43 million grant. Another \$130 million may follow as research continues. The Army also disclosed plans to award Sanofi an exclusive license to a pair of patents that are crucial to the vaccine.

But this move upset some lawmakers and patient advocates, who fear the deal will give the company a monopoly to exploit — and might lead Sanofi to jack up prices for American consumers, assuming the virus spreads and vaccines actually become a big market.

The backdrop to such concerns is the larger controversy over the rising cost of prescription medicines, a problem that has upset many Americans, prompted a flurry of legislation, and put the pharmaceutical industry on the defensive.

Sanofi, which is already under fire over its insulin pricing, is well-aware of the problem. Earlier this month, the company sought to deflect criticism — and mounting negative publicity — by vowing to limit price hikes for its medicines to a level at or below the rate of medical inflation in the US.

But an advocacy group, Knowledge Ecology International, argued Sanofi cannot be trusted and pointed to pricing for its Aubagio multiple sclerosis drug. Americans using a coupon can pay about \$6,100 for a month's supply — which is seven times more than patients pay in France and at least four times the price in the UK, Ireland, and Australia. A Sanofi spokeswoman says prices vary due to circumstances in each country.

This is why Senator Bernie Sanders and others maintain the Army should push Sanofi for fair pricing on the Zika vaccine. They want a guarantee that Americans would pay a price comparable to what other countries are charged. But as you know, Secretary Speer, Sanofi rejected such a request from your staff last month.

Drug makers generally avoid discussing pricing decisions in advance and Sanofi is no exception. In this case, the company has noted the vaccine doesn't even exist yet.

A Sanofi executive offered further insight in a letter to a House subcommittee last week. "Given the high risk nature of vaccine development and unpredictability for diseases like Zika, if the US government changes its historic approach to licensing terms, it could undermine the intent of these

types of collaborations,” wrote Adam Gluck, who heads US government relations for the drug maker.

In other words, if a company is forced to agree to certain pricing constraints in advance, it may not bother working with the government to develop such vaccines in the first place.

Indeed, this risk that companies might respond in this way has long worried government officials. In 1995, in fact, the National Institutes of Health removed what was called a “reasonable pricing” clause from research agreements with companies. At the time, former NIH Director Harold Varmus described such clauses as a “restraint” on new product development.

“What companies don’t like is additional uncertainty for commercial considerations piled on top of the inherent risk of doing drug development,” said Genia Long, a senior advisor at Analysis Group, an economic and strategic consulting firm. “If the federal government is going to insert pricing considerations, it might affect their willingness to enter into such agreements.”

I understand that such notions may give your negotiating team second thoughts. Playing hardball in a situation where public health is at stake is not easy.

But while you may be worried that Sanofi could walk away if pressed too hard on pricing, consider that the company also has something to lose — it would be turning its back on a potentially money-making vaccine that can be sold in numerous markets around the world.

In an era of rising drug costs — an issue that your boss has insisted must be solved — you have an opportunity to ensure that tax dollars spent subsidizing research provide a return on investment that benefits all Americans.

Questions from Ed Silverman at STAT:

Why is an exclusive license going to be granted?

And will the terms be disclosed?

NIAID Response (attributed generally to NIAID):

b5

From: Stevens, Ashley J [astevens@bu.edu]
Sent: 6/13/2017 9:55:34 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=OD/cn=ROHRBAUM]
Subject: Final Draft
Attachments: **b4**

Thanks so much for the RePORTER tutorial. You'll see I made effective use of it.

Best wishes,

Ashley Stevens
Focus IP Group, LLC
Winchester, MA

Office: (781) 721-2670
Cell: **b6**

b4

From: Lambert, Richard (NIH/NIAID) [C] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=9668E9326D084AC893665B084FD4FE-LAMBERTR]
Sent: 5/16/2019 11:43:51 AM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718ccb29fab-rohrbaum]
Subject: FW: IPWatchdog: "Jamie Love Responds to Criticism of Knowledge Ecology International Letter"

FYI

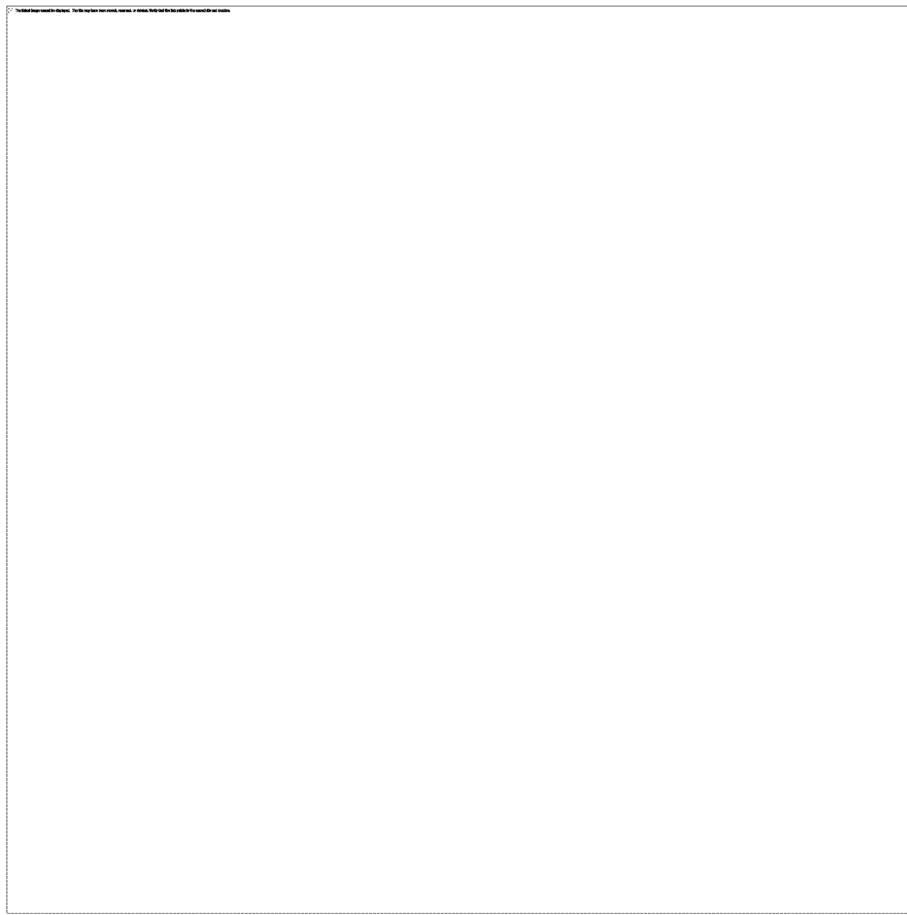
Richard A. Lambert
Contractor
National Institute of Allergy and Infectious Diseases
National Institutes of Health
U.S. Department of Health and Human Services
5601 Fishers Lane, Rm. 2G47, MSC 9804
Bethesda, MD 20892-9804
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301.496.2644 main officeline
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From: IPWatchdog.com <noreply@ipwatchdog.com>
Sent: Thursday, May 16, 2019 5:04 AM
To: Lambert, Richard (NIH/NIAID) [C] <lambertr@niaid.nih.gov>
Subject: IPWatchdog: "Jamie Love Responds to Criticism of Knowledge Ecology International Letter"

Patents, Software Patents, Patent Applications & Patent Law

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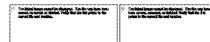
Jamie Love Responds to Criticism of Knowledge Ecology International Letter

By James Love on May 15, 2019 04:15 pm

On May 12, Frederick Reinhart published an article titled "Knowledge Ecology International Letter Misleads on March-In Rights." Reinhart is a past president of the Association of University Technology Managers (AUTM), and his views echo those expressed by many in the university technology transfer field, including a frustration that not everyone acknowledges and appreciates the considerable

investments and risks undertaken by the for-profit companies that license patents to inventions funded by the federal government. Knowledge Ecology International (KEI) recognizes the importance of the private sector in bringing therapies to the market, even when federal funding of R&D has played a role, and also that robust returns on those investments have a positive impact on innovation.

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House IP Subcommittee Discusses Section 101, Fraudulent Chinese Trademark Applications During USPTO Oversight Hearing

By Steve Brachmann on May 15, 2019 12:15 pm

Last week, the House Committee on the Judiciary's Subcommittee on Courts, Intellectual Property, and the Internet convened a hearing to perform oversight of the U.S. Patent and Trademark Office. USPTO Andrei Iancu fielded questions on Section 101 patent eligibility issues and fraudulent trademark application filings and, while several Representatives on the subcommittee noted Director Iancu's procedural changes at the Patent Trial and Appeal Board (PTAB), much of the previous backlash to those changes seemed to have dissipated. In his opening statement, Representative Hank Johnson (D-GA), Chairman of the House IP Subcommittee, discussed the impact that issued patents have on small businesses, noting that the first patent granted to a startup results in the business both hiring an average of 16 employees and earning an average of \$10.6 million in additional sales within five years. However, Johnson added that recent case law from the U.S. Supreme Court have resulted in major issues with patent eligibility under 35 U.S.C. § 101, threatening innovation in critical technology areas like medical diagnostics. He was also concerned by a rise in fraudulent trademark filings coming from China that can hurt American businesses trying to register legitimate marks.

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Patent Trends Study Part Eleven: Cleantech Industry

By Thomas Franklin on May 15, 2019 08:15 am

Yesterday, we discussed patenting trends in artificial intelligence (AI). Today, we turn to the cleantech and green tech industries, which are changing many established industries in different sectors of the economy, as well as providing entirely new areas to innovate. Cleantech innovation is relatively steady in recent years after a growth spurt that started nearly a decade ago. Those early growth trends were likely driven by government stimulus funds that have disappeared along with the growing innovation trend. The promise of a green revolution powered by cleantech may still be happening, but it simply is not a patent growth area in general except for a few areas explored below. Developing new products in this space takes years and there are many factors that interrupt this cycle to make product introduction difficult.

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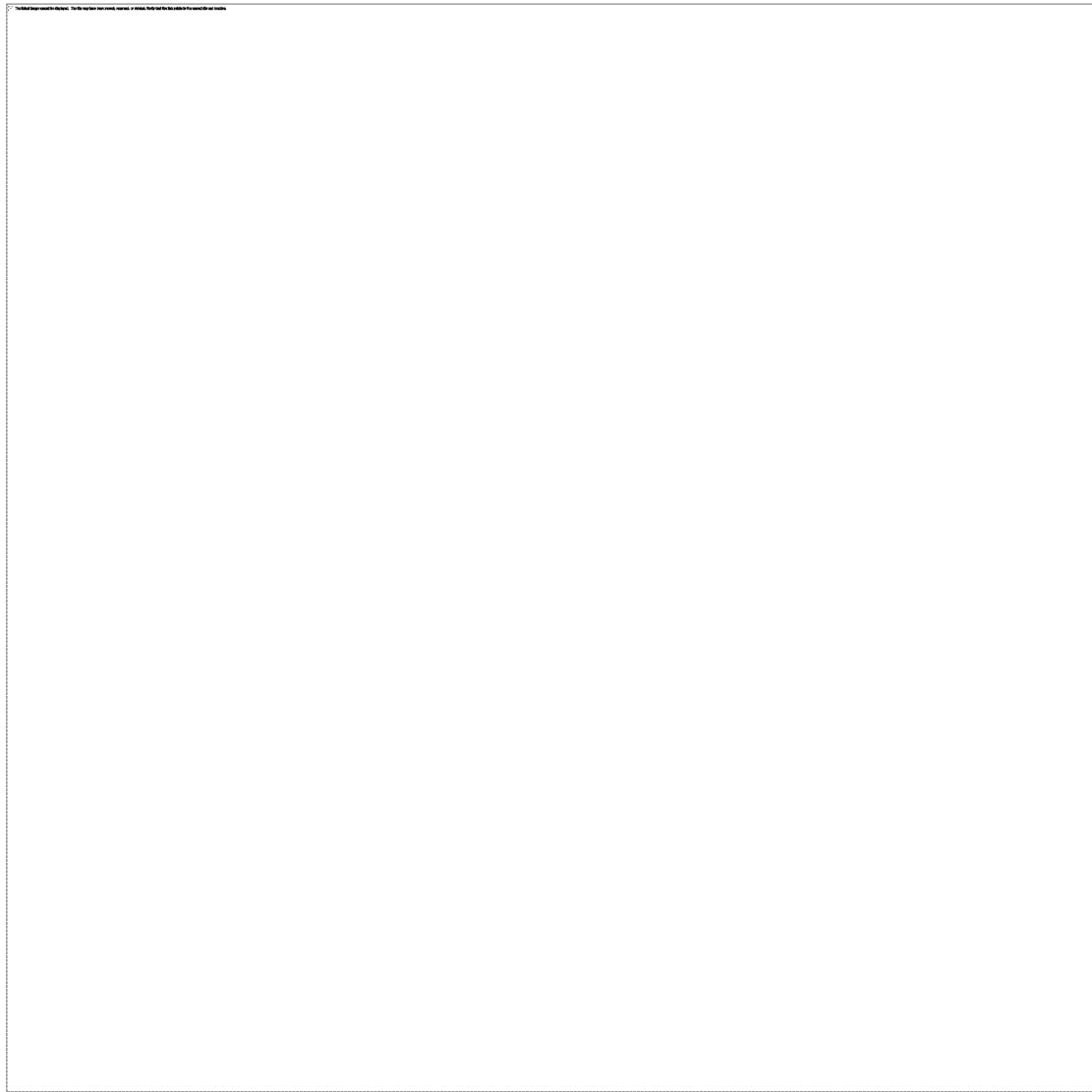
[The Price of Price Controls: Innovation Likely to Suffer in Drug Pricing Debate](#)

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[CBD Wins with USPTO's New Examination Guide for Cannabis Marks, but Lawful Use Requirements Remain Intact](#)

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By A Calendar Event On IPWatchdog on May 16, 2019 05:30 pm

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Certified Patent Valuation Analyst Training

By A Calendar Event On IPWatchdog on May 20, 2019 09:00 am

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Patent Practice Training: An Introduction to Patent Prosecution

By Gene Quinn on May 20, 2019 07:00 pm

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By Renee C. Quinn on May 23, 2019 12:00 pm

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Free Webinar: The Great Equalizer: Democratizing Innovation with Big Data and IP Analytics

By Renee C. Quinn on May 30, 2019 12:00 pm

[View Event »](#)

Valuation of Emerging Technologies

By A Calendar Event On IPWatchdog on Jun 03, 2019 09:00 am

[View Event »](#)

10th Annual Ethics in the Practice of Intellectual Property Law

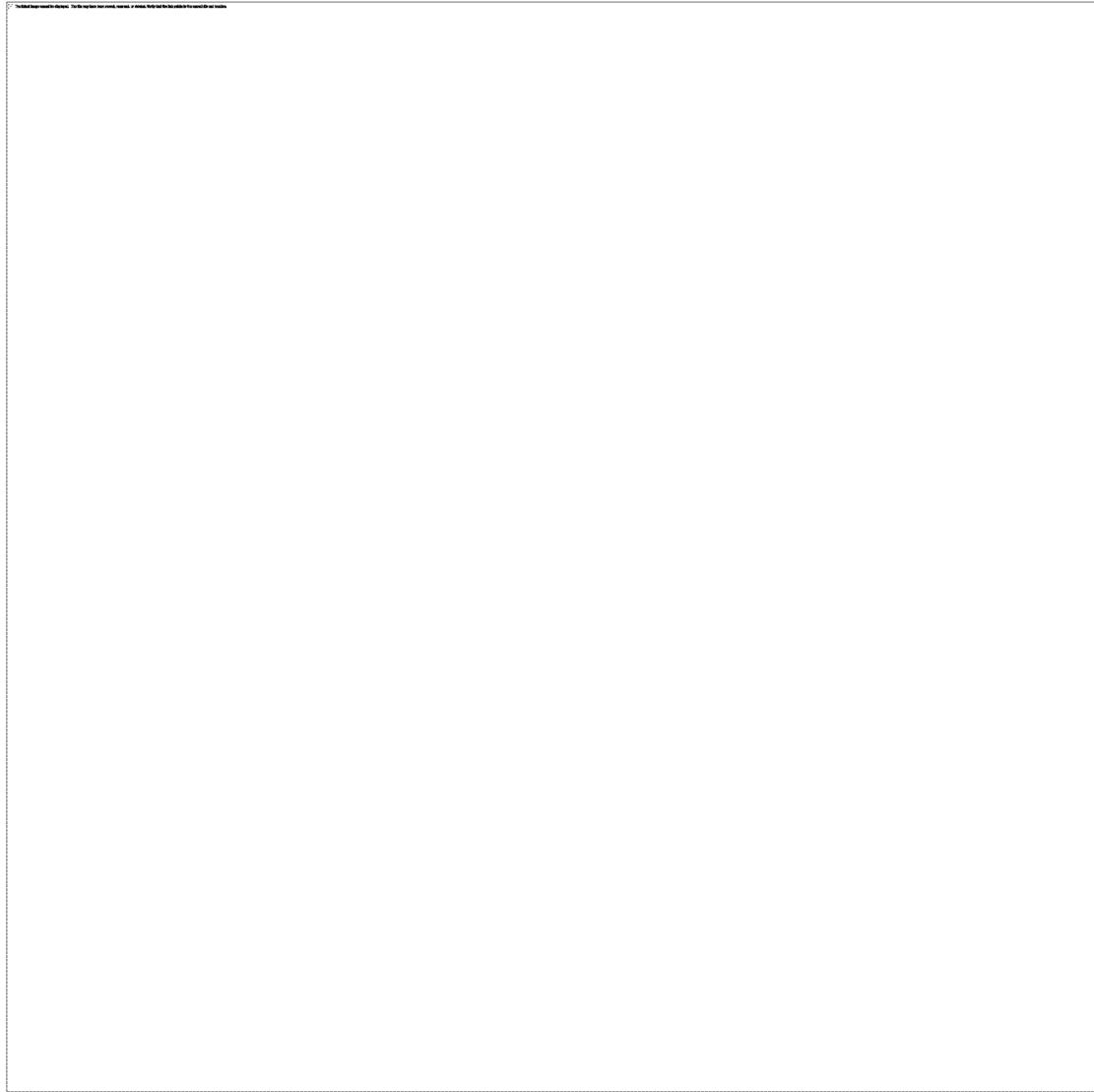
By A Calendar Event On IPWatchdog on Jun 07, 2019 12:40 pm

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Dissecting Alice at Five: The Good, the Bad and the Ugly

By Gene Quinn on Jun 20, 2019 02:00 pm

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From: Soukas, Peter (NIH/NIAID) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=B1F6020157AC47948C6E34166B78E433-SOUKASP]
Sent: 1/10/2019 2:23:57 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
CC: Puglielli, Maryann (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=9f53ceacaf754875a948081bac5cc66a-pugliellim]; Williams, Richard (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=e5f89fe4d27a43abb936bb20efeca3b9-rwilliams]; Frisbie, Suzanne (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=c402740ceaad4d4f97a8c28f16fbb349-frisbies]; Mowatt, Michael (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=cb1ef7e2e54b4164ae34814574bda638-mmowatt]
Subject: RE: My VM was about the RSV pending license

Dear Mark,

Thanks for your voicemail and email. We hope everything is going well with you. We are working on a response and will run it by you and Dale prior to providing it to KEI/MSF. Do you want to have a call to discuss the response? Thank you.

Peter Soukas
National Institutes of Health
National Institute of Allergy and Infectious Diseases
Phone: 301-594-8730
Email: ps193c@nih.gov

From: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Sent: Wednesday, January 9, 2019 3:50 PM
To: Soukas, Peter (NIH/NIAID) [E] <peter.soukas@nih.gov>
Subject: My VM was about the RSV pending license

Mark L. Rohrbaugh, Ph.D., J.D.
Special Advisor for Technology Transfer
Director, Division of Technology Transfer and Innovation Policy
Office of Science Policy
Office of the Director
National Institutes of Health

From: Berkley, Dale (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=5EE461C29F5045A49F0ADF82CAAA2F31-BERKLEYD]
Sent: 7/23/2018 6:44:14 PM
To: Freel, Rose (NIH/NCI) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=e8ae9aab7e3249e881bb573e9a189036-freelrm]; Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718ccb29fab-rohrbaum]
CC: Rodriguez, Richard (NIH/NCI) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=8092cb5394e04733ac0d4d84d25f65e5-rodrig]
Subject: RE: Prospective Grant of an Exclusive Patent License: Development of an Anti-Mesothelin Chimeric Antigen Receptor (CAR) for the Treatment of Human Cancer to Atara Biotherapeutics Inc.
Attachments: KEIComments_DRAFTresponse_7.20.2018--OGCBerkleyComments.doc

I think this is good Rose, just a couple edits for your and Mark's consideration in the attached.

Dale D. Berkley, Ph.D., J.D.
Office of the General Counsel, PHD, NIH Branch
Bldg. 31, Rm. 47
Bethesda, MD 20892
301-496-6043
301-402-2528(Fax)

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From: Freel, Rose (NIH/NCI) [E]
Sent: Monday, July 23, 2018 2:08 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Cc: Berkley, Dale (NIH/OD) [E] <berkleyd@od.nih.gov>; Rodriguez, Richard (NIH/NCI) [E] <richard.rodriguez@nih.gov>
Subject: RE: Prospective Grant of an Exclusive Patent License: Development of an Anti-Mesothelin Chimeric Antigen Receptor (CAR) for the Treatment of Human Cancer to Atara Biotherapeutics Inc.

Hi Mark & Dale,

I've put together a draft response to KEI's comments. Could you please look at the attached and let me know any edits or comments?

Thanks!
Rose

--
Rose Santangelo Freel, Ph.D.
Senior Technology Transfer Manager
National Cancer Institute
P 301-624-1257 | rose.freel@nih.gov

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Thursday, July 19, 2018 2:55 PM
To: Freel, Rose (NIH/NCI) [E] <rose.freel@nih.gov>
Cc: Rodriguez, Richard (NIH/NCI) [E] <richard.rodriguez@nih.gov>; Berkley, Dale (NIH/OD) [E] <BerkleyD@OD.NIH.GOV>
Subject: RE: Prospective Grant of an Exclusive Patent License: Development of an Anti-Mesothelin Chimeric Antigen Receptor (CAR) for the Treatment of Human Cancer to Atara Biotherapeutics Inc.

I agree with Dale with a suggestion.

b5

b5

REL0000024421

From: Freel, Rose (NIH/NCI) [E]
Sent: Thursday, July 19, 2018 8:05 AM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Cc: Rodriguez, Richard (NIH/NCI) [E] <richard.rodriguez@nih.gov>; Berkley, Dale (NIH/OD) [E] <berkleyd@od.nih.gov>
Subject: RE: Prospective Grant of an Exclusive Patent License: Development of an Anti-Mesothelin Chimeric Antigen Receptor (CAR) for the Treatment of Human Cancer to Atara Biotherapeutics Inc.

Hi Mark,

Just following up on this, let me know your thoughts on a response to KEI.

Thanks!

Rose

--

Rose Santangelo Freel, Ph.D.
Senior Technology Transfer Manager
National Cancer Institute
P 301-624-1257 | rose.freel@nih.gov

From: Freel, Rose (NIH/NCI) [E]
Sent: Tuesday, July 17, 2018 8:11 AM
To: Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>
Cc: Rodriguez, Richard (NIH/NCI) [E] <richard.rodriguez@nih.gov>; Berkley, Dale (NIH/OD) [E] <BerkeleyD@OD.NIH.GOV>
Subject: FW: Prospective Grant of an Exclusive Patent License: Development of an Anti-Mesothelin Chimeric Antigen Receptor (CAR) for the Treatment of Human Cancer to Atara Biotherapeutics Inc.

Hi Mark,

Attached are comments I received from KEI on the FR Notice for the Prospective Grant to Atara. Can you please tell me if and how we should respond?

Thanks!

Rose

--

Rose Santangelo Freel, Ph.D.
Senior Technology Transfer Manager
National Cancer Institute
P 301-624-1257 | rose.freel@nih.gov

From: James Love <james.love@keionline.org>
Sent: Friday, July 13, 2018 4:45 PM
To: Freel, Rose (NIH/NCI) [E] <rose.freel@nih.gov>
Cc: Tim Reed <Tim@haiweb.org>; Luis Gil Abinader <luis.gil.abinader@keionline.org>; Merith Basey <merith@essentialmedicine.org>; Alex Lawson <alawson@socialsecurityworks.org>; Fran Quigley <fran.quigley@socialsecurityworks.org>; Brook Baker, Baker, Brook <b.baker@northeastern.edu>; Meg Jones-Monteiro <mjonesmonteiro@iccr.org>; Manon Ress <MANON.RESS@cancerunion.org>; Claire Cassedy <claire.cassedy@keionline.org>; Thiru Balasubramaniam <thiru@keionline.org>
Subject: Re: Prospective Grant of an Exclusive Patent License: Development of an Anti-Mesothelin Chimeric Antigen Receptor (CAR) for the Treatment of Human Cancer to Atara Biotherapeutics Inc.

Dear Dr. Freel,

REL0000024421

I'm attaching a corrected copy of the comments. The difference was just the spelling of CFR, which had been transposed in the earlier version.

Jamie

On Fri, Jul 13, 2018 at 4:09 PM, James Love <james.love@keionline.org> wrote:

Dr. Freel,

Attached are comments on the Atara license from:

Health Action International (HAI)

Health GAP

Interfaith Center on Corporate Responsibility (ICCR)

Knowledge Ecology International (KEI)

People of Faith for Access to Medicines (PFAM)

Social Security Works (SSW)

Union for Affordable Cancer Treatment (UACT)

Universities Allied for Essential Medicines (UAEM)

--
James Love. Knowledge Ecology International

<http://www.keionline.org/donate.html>

KEI DC tel: +1.202.332.2670, US Mobile: +1.202.361.3040, Geneva Mobile: +41.76.413.6584, twitter.com/jamie_love

--
James Love. Knowledge Ecology International

<http://www.keionline.org/donate.html>

KEI DC tel: +1.202.332.2670, US Mobile: +1.202.361.3040, Geneva Mobile: +41.76.413.6584, twitter.com/jamie_love

b5

b5

From: Chang, Kevin (NIH/NCI) [E] [/O=NIH/OU=EXTERNAL
(FYDIBOHF25SPDLT)/CN=RECIPIENTS/CN=EC1C6145EC1648F3B642215B9E72B16A]
Sent: 7/7/2017 8:38:06 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=OD/cn=ROHRBAUM]; Rodriguez, Richard (NIH/NCI)
[E] [/O=NIH/OU=EXTernal (FYDIBOHF25SPDLT)/cn=Recipients/cn=5c43750192ca4e0e890422519477dd41];
Finkelstein, Lisa (NIH/NCI) [E] [/O=NIH/OU=EXTernal
(FYDIBOHF25SPDLT)/cn=Recipients/cn=7dff1c776a604bb9a2ca90db383ea99a]
Subject: RE: RE: Prospective Grant of Exclusive Patent License: Chimeric L1/L2 Protein and Virus-Like Particles Based Human
Papillomavirus Vaccines
Attachments: NIH Response Letter2.docx

Hi Mark,

Thanks for the suggestion, I have revised the letter based on your comments. Please let me know if there are any other comments.

Best regards,

Kevin

Kevin W. Chang, Ph.D.
Senior Technology Transfer Manager
NCI Technology Transfer Center
9609 Medical Center Dr.
Room 3W-128, MSC 9702
Rockville, MD 20850-9702
Phone: 240-276-6910
Email: changke@mail.nih.gov

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From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Friday, July 07, 2017 4:24 PM
To: Chang, Kevin (NIH/NCI) [E] <changke@mail.nih.gov>; Rodriguez, Richard (NIH/NCI) [E] <richard.rodriguez@nih.gov>;
Finkelstein, Lisa (NIH/NCI) [E] <lfinkels@mail.nih.gov>
Subject: RE: RE: Prospective Grant of Exclusive Patent License: Chimeric L1/L2 Protein and Virus-Like Particles Based
Human Papillomavirus Vaccines

Thanks Kevin, just a small suggestion. [redacted]

b5

b5

From: Chang, Kevin (NIH/NCI) [E]
Sent: Friday, July 07, 2017 4:10 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>; Rodriguez, Richard (NIH/NCI) [E] <richard.rodriguez@nih.gov>; Finkelstein, Lisa (NIH/NCI) [E] <lfinkels@mail.nih.gov>
Subject: RE: RE: Prospective Grant of Exclusive Patent License: Chimeric L1/L2 Protein and Virus-Like Particles Based Human Papillomavirus Vaccines

Hi Mark, Richard, and Lisa,

This is the response letter that I plan to send to KEI in response to their comments for this intent to grant. Please let me know if you have any comments.

Best regards,

Kevin

Kevin W. Chang, Ph.D.
Senior Technology Transfer Manager
NCI Technology Transfer Center
9609 Medical Center Dr.
Room 3W-128, MSC 9702
Rockville, MD 20850-9702
Phone: 240-276-6910
Email: changke@mail.nih.gov

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From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Tuesday, June 06, 2017 3:42 PM
To: Chang, Kevin (NIH/NCI) [E] <changke@mail.nih.gov>
Subject: RE: RE: Prospective Grant of Exclusive Patent License: Chimeric L1/L2 Protein and Virus-Like Particles Based Human Papillomavirus Vaccines

Thanks. Are you going to draft a response? I would like to see it before it goes out please.

From: Chang, Kevin (NIH/NCI) [E]
Sent: Tuesday, June 06, 2017 3:41 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>
Subject: FW: RE: Prospective Grant of Exclusive Patent License: Chimeric L1/L2 Protein and Virus-Like Particles Based Human Papillomavirus Vaccines

Hi Mark,

Just wanted to let you know that KEI sent comments for my Intent to Grant Federal Register Notice. Please see the emails below. The federal register notice is in the following link.

<https://www.federalregister.gov/documents/2017/05/19/2017-10153/prospective-grant-of-exclusive-patent-license-chimeric-l1l2-protein-and-virus-like-particles-based>

Best,

Kevin

Kevin W. Chang, Ph.D.
Senior Technology Transfer Manager
NCI Technology Transfer Center
9609 Medical Center Dr.
Room 3W-128, MSC 9702
Rockville, MD 20850-9702
Phone: 240-276-6910
Email: changke@mail.nih.gov

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From: Rodriguez, Richard (NIH/NCI) [E]
Sent: Tuesday, June 06, 2017 3:29 PM
To: Chang, Kevin (NIH/NCI) [E] <changke@mail.nih.gov>
Subject: RE: RE: Prospective Grant of Exclusive Patent License: Chimeric L1/L2 Protein and Virus-Like Particles Based Human Papillomavirus Vaccines

Yes

From: Chang, Kevin (NIH/NCI) [E]
Sent: Tuesday, June 06, 2017 2:48 PM
To: Rodriguez, Richard (NIH/NCI) [E] <richard.rodriguez@nih.gov>
Subject: FW: RE: Prospective Grant of Exclusive Patent License: Chimeric L1/L2 Protein and Virus-Like Particles Based Human Papillomavirus Vaccines

Hi Richard,

Just wanted to let you know that I received comments from KEI from my intent to grant Federal Register notice. Should I also forward this to Mark, so he is aware of this?

Kevin W. Chang, Ph.D.
Senior Technology Transfer Manager
NCI Technology Transfer Center
9609 Medical Center Dr.
Room 3W-128, MSC 9702
Rockville, MD 20850-9702
Phone: 240-276-6910
Email: changke@mail.nih.gov

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From: jamespackardlove@gmail.com [mailto:jamespackardlove@gmail.com] **On Behalf Of** Jamie Love

Sent: Monday, June 05, 2017 4:25 PM

To: Chang, Kevin (NIH/NCI) [E] <changke@mail.nih.gov>

Cc: Manon Ress <MANON.RESS@cancerunion.org>

Subject: RE: Prospective Grant of Exclusive Patent License: Chimeric L1/L2 Protein and Virus-Like Particles Based Human Papillomavirus Vaccines

June 5, 2017

Kevin W. Chang, Ph.D.
Senior Technology Transfer Manager
NCI Technology Transfer Center
9609 Medical Center Drive,
RM 1E530 MSC 9702
Bethesda, MD 20892-9702
Telephone: (240)-276-6910;
Facsimile: (240)-276-5504;

Via Email: changke@mail.nih.gov.

RE: Prospective Grant of Exclusive Patent License: Chimeric L1/L2 Protein and Virus-Like Particles Based Human Papillomavirus Vaccines

We are writing in response to the notice in 82 FR 23012

, regarding the possible grant of an exclusive license to PathoVax, LLC located in Baltimore, MD

for
patents relating to
Chimeric L1/L2 Protein and Virus-Like Particles Based Human Papillomavirus Vaccines

It is our understanding that PathoVax is a very small start-up, that has been funded by the NIH and a handful of investors. We would like to know the extent of the NIH funding of the firm, prior to the license, and also the extent to which the US government will be funding the clinical trials related to the licensed patents.

We are particularly interested in this human papillomavirus (HPV) vaccine

, because the costs of the existing vaccines have been high, and access has been limited, both in the United States and elsewhere.

In the past, exclusive licenses of federally funded patented related to the HPV vaccines have created unfortunate barriers to the development of vaccines that protect against the widest range of HPV strains.

According the NIH [1], HPVs causes several types of cancer, including:

- **Cervical cancer:** Virtually all cases of cervical cancer are caused by HPV, and just two HPV types, 16 and 18, are responsible for about 70% of all cases (7, 8).
- **Anal cancer:** About 95% of anal cancers are caused by HPV. Most of these are caused by HPV type 16.
- **Oropharyngeal cancers (cancers of the middle part of the throat, including the soft palate, the base of the tongue, and the tonsils):** About 70% of oropharyngeal cancers are caused by HPV. In the United States, more than half of cancers diagnosed in the oropharynx are linked to HPV type 16 (9).
- **Rarer cancers:** HPV causes about 65% of vaginal cancers, 50% of vulvar cancers, and 35% of penile cancers (10). Most of these are caused by HPV type 16.

High-risk HPV types cause approximately 5% of all cancers worldwide (11). In the United States, high-risk HPV types cause approximately

3% of all cancer cases among women and 2% of all cancer cases among men (12).

The vaccine should be available and affordable to all.

Question: Has the NIH done an analysis to see if a policy of non-exclusive licensing would better serve the goals of developing vaccines with the widest range of protection for HPV strains?

As regards pricing and access, it is our view that the NIH is required under 35 USC 209 and 35 USC 201(f) to ensure that any holder of an exclusive license will make the vaccine available to the public on reasonable terms.

One condition on pricing that is essential is that the price of the vaccine in the United States be no higher than the companies charge in other high income countries. To this end, language that requires that the price of the vaccine in the United States be no more than the median price of the vaccine in the seven countries with the highest GDP and a per capita income of at least 50 percent of the US per capital income, can and should be inserted into the patent license. This is a very minimal protection for U.S. residents, who after, all, have paid for the patented invention.

Secondly, it is important to ensure that the vaccine is available at prices that are affordable in developing countries. To this end, we suggest the following language in the license agreement:

A vaccine based upon the patented inventions shall be available at prices that are affordable in countries with per capita incomes of 30 percent or less of the United States, and if the U.S. Department of Health and Human Services finds otherwise, it reserves the right to grant non-exclusive to generic vaccine manufacturers.

We requests that the license require PathoVax to provide the NIH annual reports on the R&D outlays related to the patents, including expenditures on each specific clinical trial, and annual reports providing the revenues from sales, the number of units sold, and prices per unit, and the royalties paid to the United States government, in each country where the products are commercialized, and that these reports be made public.

Sincerely,

James Love, Knowledge Ecology International
Manon Ress, PhD. Union for Affordable Cancer Treatment

[1] <https://www.cancer.gov/about-cancer/causes-prevention/risk/infectious-agents/hpv-fact-sheet>

--

James Love. Knowledge Ecology International
<http://www.keionline.org/donate.html>
KEI DC tel: +1.202.332.2670, US Mobile: +1.202.361.3040, Geneva Mobile: +41.76.413.6584,
twitter.com/jamie_love

b5

From: Berkson, Laura (NIH/OD) [E] [/O=NIH/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=DAMIANOLD]
Sent: 6/14/2017 6:39:15 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=OD/cn=ROHRBAUM]
CC: Culhane, Ned (NIH/OD) [E] [/O=NIH/OU=Nihexchange/cn=recipients/cn=culhane]
Subject: Lawmakers ask U.S. Army to hold a hearing on Zika vaccine licensing
Attachments: FL Letter to Army re Zika Vaccine - Fully Executed.pdf

FYI: <https://www.statnews.com/pharma/2017/06/14/lawmakers-army-zika-vaccine/>. NIH is mentioned at the end of the article.

Lawmakers ask U.S. Army to hold a hearing on Zika vaccine licensing

By [ED SILVERMAN](#) @PharmaLot
JUNE 14, 2017

A group of Florida lawmakers is urging the U.S. Army to hold a hearing on its plan to give Sanofi an exclusive license to develop a Zika virus vaccine, a move that has raised concerns the product may be priced too high for many Americans, even though it was developed with taxpayer funds.

In a June 13 letter, eight U.S. House Democrats and one Republican expressed concern about the “potential for monopolistic practices that would, effectively, keep this life-saving vaccine out of reach for far too many of our constituents.” At the same time, U.S. Sen. Bill Nelson, who is also a Democrat, sent his own letter in which he urged the Army to limit the price for the vaccine.

Both missives noted that Sanofi, which is one of the world’s largest vaccine makers, has already won a \$43 million government grant and stands to receive another \$130 million to run late-stage trials. Consequently, the representatives argued that awarding an exclusive license to the company would add “insult to injury,” and they want the Army to explain how such a license is reasonable or necessary.

This the second time in recent weeks that lawmakers from a Gulf state have decried plans for an exclusive license. Last month, Louisiana Gov. John Edwards warned Acting U.S. Army Secretary Robert Speer that if the mosquito-borne virus spreads, the possibility of monopoly pricing “could cripple state budgets and threaten public health.”

The letters may ratchet up the pressure on the Army to change course amid cries from still other lawmakers and consumer advocates to demand that Sanofi agree to some kind of pricing agreement as part of any licensing deal. As we reported recently, however, the company in April rejected such a request from the Army, although overall licensing talks are still under way.

We asked the Army if a hearing will be scheduled and we will update you accordingly.

The episode highlights a growing debate about the extent to which drug makers should be allowed to benefit from products that are developed — at least in part — with taxpayer funds. In this instance, the lawmakers and consumer advocates are concerned over speculation that, if the virus spread quickly, Sanofi will have a lock on a potentially lucrative market.

One group, Knowledge Ecology International, argued Sanofi cannot be trusted and pointed to pricing for its Aubagio multiple sclerosis drug. Americans using a coupon can pay about \$6,100 for a month's supply — which is seven times more than patients pay in France and at least four times the price in the UK, Ireland, and Australia. Sanofi countered that prices vary due to circumstances in each country.

The advocacy group has also made a point of citing federal law indicating exclusive licensing should be made only to serve a public benefit. But in a recent letter to U.S. Sen. Bernie Sanders, Robert Speer, noted that only Sanofi was “willing to license” this specific discovery, prompting concern that the Army is unwilling to push the company about pricing over fears it may walk away.

For its part, Sanofi has said that a price has not yet been set, but one executive maintained that royalties would be paid. Meanwhile, in a May 22 letter to a Congressional subcommittee, another Sanofi executive insisted the company is not pursuing the project based on a “commercial return” and intends to price the vaccine in order to “facilitate access” in the interest of public health.

Moreover, Adam Gluck, who heads U.S. government relations at Sanofi, noted that the company delayed other R&D programs to speed development of the vaccine out of a “sense of corporate responsibility” to address a potential public health crisis. But he also warned that, “given the high-risk nature of vaccine development unpredictability for diseases like Zika, if the U.S. government changes its historic approach to licensing terms, it could undermine the intent of these types of collaborations.”

His language raised debate over whether the federal government should reinstate language in research agreements that contain “reasonable pricing.” This requirement was removed by the U.S. National Institutes of Health in 1995 over concerns that such clauses would be seen by industry as a “restraint” on new product development.

Congress of the United States

Washington, DC 20515

June 13, 2017

Mr. Robert M. Speer
Acting Secretary of the Army
101 Army Pentagon
Washington, D.C. 20301-1400

RE: Zika Vaccine Agreement

Dear Secretary Speer:

As Members of Congress representing Florida, we write to you regarding the proposed exclusive license of patents on a Zika vaccine from the U.S. Army to Sanofi Pasteur through the year 2036, without addressing concerns of affordability.

According to the Centers for Disease Control and Prevention (CDC), Florida experienced 1,115 laboratory-confirmed symptomatic cases of the Zika virus in 2016, and 5,102 symptomatic cases of Zika were reported nationwide.¹ With the summer months upon us, we brace for another mosquito season and hope it is better than the last. However, we owe it to our constituents to do more than just hope – we must proactively ensure that our government is taking all necessary steps to protect Americans from the Zika virus.

To that end, we are very concerned about reports that the Army is planning to exclusively license French pharmaceutical company, Sanofi Pasteur, to manufacture a Zika vaccine that has been developed at the Walter Reed Army Institute of Research since March of 2016. As Members representing Florida, we are especially concerned of the potential for monopolistic practices that would effectively keep this lifesaving vaccine out of reach for far too many of our constituents.

Adding insult to injury, this vaccine has been created with millions of dollars of federal funding. Taxpayers, who have endowed the research and development of a Zika vaccine that would keep Americans Zika-free and prevent deadly birth defects in babies, should be protected from high prices; not forced to pay more than anyone else around the globe. Walter Reed and the National Institutes of Health have done all of the pre-clinical research, and are currently doing Phase I clinical trials. Sanofi has also received a Department of Health and Human Services Biomedical Advanced Research and Development Authority grant of \$43 million for Phase II trials with an option for \$130 million for Phase III trials if needed.²

¹ <https://www.cdc.gov/zika/reporting/2016-case-counts.html>

² <https://wayback.archive-it.org/3926/20170127192443/https://www.hhs.gov/about/news/2016/09/26/barda-awards-funding-speed-development-zika-vaccine.html>

As the benefactors of this vital scientific research, Americans deserve to know how an exclusive license is either a reasonable or necessary incentive to bring the product to market in this particular instance, as required under 35 U.S.C. § 209; and at a minimum, Americans deserve binding assurances from Sanofi that U.S. residents will not pay more than residents of other high-income nations. Accordingly, we urge you to (1) hold a public hearing on the proposed license so that the public and Sanofi may address concerns over the pricing of the vaccine, and (2) delay the decision regarding the exclusive license on the patent until after such public hearing has been held.

Our constituents know the repercussions of the Zika virus, and stand to suffer physically and financially in the event of an outbreak. For instance, the per-child lifetime medical and indirect Zika costs have been estimated by the CDC to be as high as \$10 million.³ We are eager to see a Zika vaccine come to market, but if the vaccine is unaffordable, the results will be devastating, and in some cases, deadly, for our constituents. We look forward to your prompt response.

Sincerely,

Debbie Wasserman Schultz

Debbie Wasserman Schultz (FL-23)
Member of Congress



Darren Soto (FL-09)
Member of Congress

Lois Frankel

Lois Frankel (FL-21)
Member of Congress

Kathy Castor

Kathy Castor (FL-14)
Member of Congress

Alice L. Hastings

Alice L. Hastings (FL-20)
Member of Congress

Theodore E. Deutch

Theodore E. Deutch (FL-22)
Member of Congress



Illeana Ros-Lehtinen (FL-27)
Member of Congress



Al Lawson (FL-05)
Member of Congress

Charlie Crist

Charlie Crist (FL-13)
Member of Congress

³ <https://www.cdc.gov/media/releases/2016/t0404-zika-summit.html>

From: Mowatt, Michael (NIH/NIAID) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=CB1EF7E2E54B4164AE34814574BDA638-MMOWATT]
Sent: 10/6/2017 4:53:18 PM
To: Gadhia, Ami (NIH/NCATS) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0fd345316c77427da92947ab04d5511c-gadhiaad]; Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718ccb29fab-rohrbaum]; Solowiej, Anna (NIH/NHGRI) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=12d161a0bbdd4090b24e61708aa61afa-solowieja]
CC: Frisbie, Suzanne (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=c402740ceaad4d4f97a8c28f16fbb349-frisbies]
Subject: RE: KEI asks HHS to use B-D right in Zinbryta patent (multiple sclerosis)

Happy to make the suggestion. When's the next meeting? I'm not available on 11 Oct.

Enjoy a nice long weekend!!

From: Gadhia, Ami (NIH/NCATS) [E]
Sent: Friday, October 6, 2017 12:49 PM
To: Mowatt, Michael (NIH/NIAID) [E] <mmowatt@niaid.nih.gov>; Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>; Solowiej, Anna (NIH/NHGRI) [E] <anna.solowiej@nih.gov>
Cc: Frisbie, Suzanne (NIH/NIAID) [E] <suzanne.frisbie@nih.gov>
Subject: RE: KEI asks HHS to use B-D right in Zinbryta patent (multiple sclerosis)

Hi Mike,

Thanks for sharing. I personally agree that this type of workshop would be topical and interesting. Would you be willing to raise this topic at our next TDC-Short meeting, so that we may take a straw poll (and solicit potential volunteers)?

Best,
Ami

From: Mowatt, Michael (NIH/NIAID) [E]
Sent: Friday, October 6, 2017 12:01 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>; Solowiej, Anna (NIH/NHGRI) [E] <anna.solowiej@nih.gov>; Gadhia, Ami (NIH/NCATS) [E] <ami.gadhia@nih.gov>
Cc: Frisbie, Suzanne (NIH/NIAID) [E] <suzanne.frisbie@nih.gov>; Mowatt, Michael (NIH/NIAID) [E] <mmowatt@niaid.nih.gov>
Subject: RE: KEI asks HHS to use B-D right in Zinbryta patent (multiple sclerosis)

Thanks for sharing this, Mark.

Anna and Ami,

I wonder whether an organized discussion of these efforts and activities over the past year or so would be beneficial for our community.

Some possible objectives for such a discussion:

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Joe Allen's talk next week will provide great background for this discussion.

We may want to consider organizing a workshop on the topic, possibly inviting outside speakers and engaging a larger audience. I think it would be a significant draw.

Mike

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Friday, October 6, 2017 10:17 AM
To: NIH TDC Short <niaaatdcs-l@mail.nih.gov>
Subject: FW: KEI asks HHS to use B-D right in Zinbryta patent (multiple sclerosis)

NOTE this product utilizes NIH licensed patents based in inventions made by NINDS and NCI scientists. The formal "March-In" proceedings of Bayh-Dole do not apply to intramural inventions. However, article 5.4b of the model exclusive license reads:

"In exceptional circumstances, and in the event that the Licensed Patent Rights are Subject Inventions made under a CRADA, the Government, pursuant to 15 U.S.C. §3710a(b)(1)(B), retains the right to require the Licensee to grant to a responsible applicant a nonexclusive, partially exclusive, or exclusive sublicense to use the Licensed Patent Rights in the Licensed Field of Use on terms that are reasonable under the circumstances, or if the Licensee fails to grant this license, the Government retains the right to grant the license itself. The exercise of these rights by the Government shall only be in exceptional circumstances and only if the Government determines:

- (i) the action is necessary to meet health or safety needs that are not reasonably satisfied by the Licensee;
- (ii) the action is necessary to meet requirements for public use specified by Federal regulations, and these requirements are not reasonably satisfied by the Licensee; or
- (iii) the Licensee has failed to comply with an agreement containing provisions described in 15 U.S.C. §3710a(c)(4)(B);

-Mark

<http://www.keionline.org/node/2867>

KEI asks HHS to use Bayh-Dole rights in Zinbryta patent (drug for multiple sclerosis)

Submitted by KEI Staff on 14. September 2017 - 12:30

- [Medical Technologies](#)

Attached is a letter sent on September 14, 2017 to Andrew Bremberg, an Assistant to the President and the Director of the Domestic Policy Council at the White House, and Keagan Lenihan, a Senior Adviser to HHS

Secretary Tom Price, regarding Zinbryta (INN: daclizumab), a drug to approved by the FDA to treat multiple sclerosis. (PDF version [here](#))

This is an older drug, and the NIH obtained a patent on its use to treat multiple sclerosis, and licensed the patent on a exclusive basis to Biogen. Biogen and Abbvie market the drug around the world. The price in the United States is more than \$96,000 per year (\$7390 per injection every 4 weeks, 13 times a year), but far lower in every high income country where KEI obtained prices.

The letter asks DHHS to use one or more of three federal rights in the NIH licensed patent to "authorize affordable competition, or to force Biogen to lower its price." The three actions include using the royalty free right in the patent, exercising march-in rights, or terminating the license. The option to terminate the license is featured in the letter, and it is an action that KEI had not focused on previously.

The termination clause is something the U.S. government can do with government owned patents, including any owned by the NIH.

At the end of this blog is a graph of the prices of MS drugs, over time.

Below is an excerpt from the beginning and another excerpt from the end of the letter.

We write to you today with regard to the excessive price of an important drug for multiple sclerosis called daclizumab, co-marketed by Biogen and AbbVie as Zinbryta at prices roughly 3 to 4 times higher in the United States than in other high income countries. The patent for Zinbryta was licensed from the NIH, and under the Bayh-Dole Act there are three specific actions the United States government can and should utilize to authorize affordable competition, or to force Biogen to lower its price. These include: (1) making use of the government's royalty-free rights in the patent; (2) utilizing the "march-in" right to license the patent to a third party; and/or (3) terminating the exclusive license.

Amidst a crisis of out-of-control drug prices, this is an instance where the federal government has the power to act without the need for any additional statutory authority.

[snip]

[snip]

The United States prices are 2.8 to 4.3 times higher than any of the reference countries. The U.S. price is 2.8 times higher than Norway and Denmark and 3.8 times higher than Switzerland, even though all three of these countries have higher per capita incomes than the United States, and the U.S. taxpayers funded the relevant discovery and own the patent.

There is no reason to accept a foreign price, even from a country of a similar per capita income, as reasonable. But in our opinion, it is unreasonable for Biogen/Abbvie to charge higher prices in the United States than in other large economies with a per capita income at least 50 percent of the United States.

In this case, prices in the U.S. are not only higher — they are 180 to 330 percent higher than every high income country where KEI could obtain pricing data. The pricing of Zinbryta is contrary to statutory requirement of the Bayh-Dole Act to make the inventions available to the public on reasonable terms.

A failure by HHS to address the discrimination against U.S. residents in pricing harms everyone who buys or reimburses the drugs, including all U.S. taxpayers, all employers who pay for health benefits, and many persons living with multiple sclerosis who face daunting co-payments, who are underinsured, or who never get the drug because of its high cost.

Conclusion

We request that the Department of Health and Human Services use one or more of the three options at its disposal under the Bayh Dole Act to lower prices of this important MS drug, including:

- (1) under 35 U.S.C. § 209(d)(1), utilizing the royalty-free license in the government-owned patent to authorize generic competition;
- (2) under 35 U.S.C. § 203(a), utilizing the “march-in” rights to license the drug to a third party; or
- (3) 35 U.S.C. § 209(d)(3), terminating the exclusive NIH license to Abbott/Biogen on the ground that the company is failing to abide by its obligation to make to invention “available to the public on reasonable terms”.

Specifically, this letter should be seen as request to exercise march-in rights under 35 U.S.C. § 203(a), and/or to terminate the license under 35 U.S.C. § 209(d)(3), on the grounds that charging U.S. residents 2.8 to 4.3 times more than residents in other high income countries is on its face unreasonable, and in violation of the requirement in 35 U.S.C. § 201(f) to make the invention covered by the license “available to the public on reasonable terms.” We also urge DHHS to use the royalty-free right in the patents to exercise leverage and freedom to operate whenever it faces challenges in implementing its section 203 or 209 rights.

We believe that terminating the exclusive license may be the best option, because it will provide the most leverage and the most flexibility in terms of obtaining alternative supplies of the product. But a credible threat to use any of these three options will be sufficient to force Biogen and AbbVie to lower its price of Zinbryta, at least to the prices that the companies already charge in other countries with incomes similar to the United States.

The Trump Administration has made numerous public pronouncements regarding the need to fight high drug prices, a policy point supported by overwhelming public opinion. In this instance, the government has all of the leverage it needs to take strong, decisive action to benefit multiple sclerosis patients, consumers, and taxpayers.

We request a meeting at your earliest convenience to discuss this matter further.

REL0000024431

From: Rodriguez, Richard (NIH/NCI) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=8092CB5394E04733AC0D4D84D25F65E5-RODRIGR]
Sent: 1/10/2019 2:00:02 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
CC: Yang, Jasmine (NIH/NCI) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=dcacd5b675e74725a0d6a6fc9a130431-yangjj2_6b5]; Thomas, Jeffrey (NIH/NCI) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=f7b9fca6f5634a45ba8802d6f6c8a410-jeffreyt]
Subject: KEI Response to Jasmine's FRN
Attachments: Ltr to KEI_2019-01-09_RL2_1-10-19.docx

Hi Mark,

We have further adjusted Jasmine's response and believe it is ready to go back to KEI.

b5

b5

b5

Please let us know if you have additional thoughts.

Thanks,

Richard

RICHARD U. RODRIGUEZ
Associate Director
Patent Agent

Technology Transfer Center
National Cancer Institute
National Institutes of Health
9609 Medical Center Drive, Rm 1E530
Bethesda, MD 20892-9702 (for business mail)
Rockville, MD 20850-9702 (for courier service/visitors)
Phone (Main Office): 240-276-5530
Direct phone: 240-276-6661
Fax 240-276-5504
richard.rodriguez@nih.gov
<https://techtransfer.cancer.gov>

"Start by doing what's necessary; then do what's possible; and suddenly you are doing the impossible" - Francis of Assisi

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b5

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From: Chang, Kevin (NIH/NCI) [E] [/O=NIH/OU=EXTERNAL
(FYDIBOHF25SPDLT)/CN=RECIPIENTS/CN=EC1C6145EC1648F3B642215B9E72B16A]
Sent: 7/7/2017 8:09:31 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=OD/cn=ROHRBAUM]; Rodriguez, Richard (NIH/NCI)
[E] [/O=NIH/OU=EXTernal (FYDIBOHF25SPDLT)/cn=Recipients/cn=5c43750192ca4e0e890422519477dd41];
Finkelstein, Lisa (NIH/NCI) [E] [/O=NIH/OU=EXTernal
(FYDIBOHF25SPDLT)/cn=Recipients/cn=7dff1c776a604bb9a2ca90db383ea99a]
Subject: RE: RE: Prospective Grant of Exclusive Patent License: Chimeric L1/L2 Protein and Virus-Like Particles Based Human
Papillomavirus Vaccines
Attachments: NIH Response Letter.docx

Hi Mark, Richard, and Lisa,

This is the response letter that I plan to send to KEI in response to their comments for this intent to grant. Please let me know if you have any comments.

Best regards,

Kevin

Kevin W. Chang, Ph.D.
Senior Technology Transfer Manager
NCI Technology Transfer Center
9609 Medical Center Dr.
Room 3W-128, MSC 9702
Rockville, MD 20850-9702
Phone: 240-276-6910
Email: changke@mail.nih.gov

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From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Tuesday, June 06, 2017 3:42 PM
To: Chang, Kevin (NIH/NCI) [E] <changke@mail.nih.gov>
Subject: RE: RE: Prospective Grant of Exclusive Patent License: Chimeric L1/L2 Protein and Virus-Like Particles Based
Human Papillomavirus Vaccines

Thanks. Are you going to draft a response? I would like to see it before it goes out please.

From: Chang, Kevin (NIH/NCI) [E]
Sent: Tuesday, June 06, 2017 3:41 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>
Subject: FW: RE: Prospective Grant of Exclusive Patent License: Chimeric L1/L2 Protein and Virus-Like Particles Based
Human Papillomavirus Vaccines

Hi Mark,

Just wanted to let you know that KEI sent comments for my Intent to Grant Federal Register Notice. Please see the emails below. The federal register notice is in the following link.

<https://www.federalregister.gov/documents/2017/05/19/2017-10153/prospective-grant-of-exclusive-patent-license-chimeric-l1l2-protein-and-virus-like-particles-based>

Best,

Kevin

Kevin W. Chang, Ph.D.
Senior Technology Transfer Manager
NCI Technology Transfer Center
9609 Medical Center Dr.
Room 3W-128, MSC 9702
Rockville, MD 20850-9702
Phone: 240-276-6910
Email: changke@mail.nih.gov

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From: Rodriguez, Richard (NIH/NCI) [E]
Sent: Tuesday, June 06, 2017 3:29 PM
To: Chang, Kevin (NIH/NCI) [E] <changke@mail.nih.gov>
Subject: RE: RE: Prospective Grant of Exclusive Patent License: Chimeric L1/L2 Protein and Virus-Like Particles Based Human Papillomavirus Vaccines

Yes

From: Chang, Kevin (NIH/NCI) [E]
Sent: Tuesday, June 06, 2017 2:48 PM
To: Rodriguez, Richard (NIH/NCI) [E] <richard.rodriguez@nih.gov>
Subject: FW: RE: Prospective Grant of Exclusive Patent License: Chimeric L1/L2 Protein and Virus-Like Particles Based Human Papillomavirus Vaccines

Hi Richard,

Just wanted to let you know that I received comments from KEI from my intent to grant Federal Register notice. Should I also forward this to Mark, so he is aware of this?

Kevin W. Chang, Ph.D.
Senior Technology Transfer Manager
NCI Technology Transfer Center
9609 Medical Center Dr.
Room 3W-128, MSC 9702
Rockville, MD 20850-9702

Phone: 240-276-6910
Email: changke@mail.nih.gov

The attached information may be confidential. It is intended only for the addressee(s) identified above. If you are not the addressee(s), or an employee or agent of the addressee(s), please note that any dissemination, distribution, or copying of this communication is strictly prohibited. If you have received this email in error, please destroy the document and notify the sender of the error. Thank you.

From: jamespackardlove@gmail.com [mailto:jamespackardlove@gmail.com] **On Behalf Of** Jamie Love
Sent: Monday, June 05, 2017 4:25 PM
To: Chang, Kevin (NIH/NCI) [E] <changke@mail.nih.gov>
Cc: Manon Ress <MANON.RESS@cancerunion.org>
Subject: RE: Prospective Grant of Exclusive Patent License: Chimeric L1/L2 Protein and Virus-Like Particles Based Human Papillomavirus Vaccines

June 5, 2017

Kevin W. Chang, Ph.D.
Senior Technology Transfer Manager
NCI Technology Transfer Center
9609 Medical Center Drive,
RM 1E530 MSC 9702
Bethesda, MD 20892-9702
Telephone: (240)-276-6910;
Facsimile: (240)-276-5504;

Via Email: changke@mail.nih.gov.

RE: Prospective Grant of Exclusive Patent License: Chimeric L1/L2 Protein and Virus-Like Particles Based Human Papillomavirus Vaccines

We are writing in response to the notice in 82 FR 23012

, regarding the possible grant of an exclusive license to PathoVax, LLC located in Baltimore, MD

for
patents relating to
Chimeric L1/L2 Protein and Virus-Like Particles Based Human Papillomavirus Vaccines
.

It is our understanding that PathoVax is a very small start-up, that has been funded by the NIH and a handful of investors. We would like to know the extent of the NIH funding of the firm, prior to the license, and also the extent to which the US government will be funding the clinical trials related to the licensed patents.

We are particularly interested in this human papillomavirus (HPV) vaccine

, because the costs of the existing vaccines have been high, and access has been limited, both in the United States and elsewhere.

In the past, exclusive licenses of federally funded patented related to the HPV vaccines have created unfortunate barriers to the development of vaccines that protect against the widest range of HPV strains.

According the NIH [1], HPVs causes several types of cancer, including:

- **Cervical cancer:** Virtually all cases of cervical cancer are caused by HPV, and just two HPV types, 16 and 18, are responsible for about 70% of all cases ([7](#), [8](#)).
- **Anal cancer:** About 95% of anal cancers are caused by HPV. Most of these are caused by HPV type 16.
- **Oropharyngeal cancers (cancers of the middle part of the throat, including the soft palate, the base of the tongue, and the tonsils):** About 70% of oropharyngeal cancers are caused by HPV. In the United States, more than half of cancers diagnosed in the oropharynx are linked to HPV type 16 ([9](#)).

- **Rarer cancers:** HPV causes about 65% of vaginal cancers, 50% of vulvar cancers, and 35% of penile cancers (10). Most of these are caused by HPV type 16.

High-risk HPV types cause approximately 5% of all cancers worldwide (11). In the United States, high-risk HPV types cause approximately 3% of all cancer cases among women and 2% of all cancer cases among men (12).
The vaccine should be available and affordable to all.

Question: Has the NIH done an analysis to see if a policy of non-exclusive licensing would better serve the goals of developing vaccines with the widest range of protection for HPV strains?

As regards pricing and access, it is our view that the NIH is required under 35 USC 209 and 35 USC 201(f) to ensure that any holder of an exclusive license will make the vaccine available to the public on reasonable terms.

One condition on pricing that is essential is that the price of the vaccine in the United States be no higher than the companies charge in other high income countries. To this end, language that requires that the price of the vaccine in the United States be no more than the median price of the vaccine in the seven countries with the highest GDP and a per capita income of at least 50 percent of the US per capital income, can and should be inserted into the patent license. This is a very minimal protection for U.S. residents, who after, all, have paid for the patented invention.

Secondly, it is important to ensure that the vaccine is available at prices that are affordable in developing countries. To this end, we suggest the following language in the license agreement:

A vaccine based upon the patented inventions shall be available at prices that are affordable in countries with per capita incomes of 30 percent or less of the United States, and if the U.S. Department of Health and Human Services finds otherwise, it reserves the right to grant non-exclusive to generic vaccine manufacturers.

We request that the license require PathoVax to provide the NIH annual reports on the R&D outlays related to the patents, including expenditures on each specific clinical trial, and annual reports providing the revenues from sales, the number of units sold, and prices per unit, and the royalties paid to the United States government, in each country where the products are commercialized, and that these reports be made public.

Sincerely,

James Love, Knowledge Ecology International
Manon Ress, PhD. Union for Affordable Cancer Treatment

[1] <https://www.cancer.gov/about-cancer/causes-prevention/risk/infectious-agents/hpv-fact-sheet>

--
James Love. Knowledge Ecology International
<http://www.keionline.org/donate.html>

KEI DC tel: +1.202.332.2670, US Mobile: +1.202.361.3040, Geneva Mobile: +41.76.413.6584,
twitter.com/jamie_love

b5

b5

b5

b5

b5

From: Stevens, Ashley J [astevens@bu.edu]
Sent: 1/23/2017 11:28:58 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=OD/cn=ROHRBAUM]
Subject: RE: do you have update on
Attachments: b4

Well, since you ask, attached is the draft of the paper I mentioned! Please review footnote 5 in particular.

Your comments on the whole thing will be greatly welcomed, and I'm only sorry you can't be a co-author.

I'm slogging through doing the indications currently. That's as far as I need to go for this paper.

Best wishes,

Ashley Stevens
Focus IP Group, LLC
Winchester, MA

Office: (781) 721-2670

Cell: b6

From: Rohrbaugh, Mark (NIH/OD) [E] [mailto:RohrBauM@od.nih.gov]
Sent: Monday, January 23, 2017 6:24 PM
To: Stevens, Ashley J <astevens@bu.edu>
Subject: do you have update on

....# drugs since last study from PSRI vs total new drugs approved from all sources, i.e. % from PSRI? Like Table 2 in NEJM

Thanks

Mark L. Rohrbaugh, Ph.D., J.D.
Special Advisor for Technology Transfer
Director, Division of Technology Transfer and Innovation Policy
Office of Science Policy
Office of the Director
National Institutes of Health

b4

From: Driscoll, Claire (NIH/NHGRI) [E] [/O=NIH/OU=NIHCHANGE/CN=NHGRI/CN=CDRISCOL]
Sent: 10/24/2016 7:53:19 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/O=NIH/OU=NIHCHANGE/cn=OD/cn=ROHRBAUM]
Subject: RE: Interview request/chlorcyclizine pricing: BuzzFeed News

No worries. I will delete.

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Monday, October 24, 2016 3:51 PM
To: Driscoll, Claire (NIH/NHGRI) [E] <cdriscol@mail.nih.gov>; Vepa, Sury (NIH/NCATS) [E] <sury.vepa@nih.gov>; Portilla, Lili (NIH/NCATS) [E] <portilll@mail.nih.gov>
Subject: Re: Interview request/chlorcyclizine pricing: BuzzFeed News

Sorry Claire, meant to copy Lili

Sent from my iPhone

On Oct 24, 2016, at 8:50 PM, Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV> wrote:

b5

Sent from my iPhone

Begin forwarded message:

From: "Fine, Amanda (NIH/OD) [E]" <amanda.fine@nih.gov>
Date: October 24, 2016 at 8:27:59 PM GMT+1
To: "Rohrbaugh, Mark (NIH/OD) [E]" <RohrBauM@OD.NIH.GOV>
Cc: "McBurney, Margaret (NIH/OD) [E]" <mmcburney@od.nih.gov>, "Hardesty, Rebecca (NIH/OD) [C]" <rebecca.hardesty@nih.gov>, "Myles, Renate (NIH/OD) [E]" <mylesr@od.nih.gov>, "Wojtowicz, Emma (NIH/OD) [E]" <emma.wojtowicz@nih.gov>
Subject: RE: Interview request/chlorcyclizine pricing: BuzzFeed News

b5

Ideally we'd want a response that is able to answer all of Dan's questions:

What are the institute's priorities when licensing these drugs?
How much progress has this licensee made on marketing this drug?
What were the results of the Phase 1 trial that NIH funded on this drug?
Some observers are asking: why grant an exclusive license to a small, unknown company with no track record of bringing drugs to market?

Thanks Mark! Hope you're not working while on vacation.

Amanda

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Monday, October 24, 2016 3:22 PM
To: Fine, Amanda (NIH/OD) [E] <amanda.fine@nih.gov>
Cc: McBurney, Margaret (NIH/OD) [E] <mmmcurney@od.nih.gov>; Hardesty, Rebecca (NIH/OD) [C] <rebecca.hardesty@nih.gov>; Myles, Renate (NIH/OD) [E] <mylesr@od.nih.gov>; Wojtowicz, Emma (NIH/OD) [E] <emma.wojtowicz@nih.gov>
Subject: Re: Interview request/chlorcyclizine pricing: BuzzFeed News

I am available

b5

b5

Sent from my iPhone

On Oct 24, 2016, at 8:10 PM, Fine, Amanda (NIH/OD) [E] <amanda.fine@nih.gov> wrote:

Greetings-

I'm including all three of you per Mark's out of office and given that the reporter's deadline is October 28.

NIDDK received the below inquiry from Dan Vergano at Buzzfeed regarding Knowledge Ecology International's (KEI) questions about the drug chlorcyclizine which had/has a small trial at the CC. Attached is a back and forth with NIDDK/NCATS that KEI got through FOIA. Dan's questions are below.

b5

b5

Thank you in advance for your input and guidance,
Amanda

Amanda Fine
Deputy, News Media Branch
National Institutes of Health
Tel: 301-496-7246
Email: amanda.fine@nih.gov
Web: <http://www.nih.gov>

NIH . . . Turning Discovery Into Health

REL0000024442

From: Payne, January (NIH/NIDDK) [E]
Sent: Monday, October 24, 2016 2:54 PM
To: OCPLPressTeam <OCPLPressTeam@od.nih.gov>; ODOCPL Interviews (NIH/OD OCPL) <ODOCPLInterviews@mail.nih.gov>
Cc: NIDDK NIDDKMEDIA (NIH/NIDDK) <niddkmedia@niddk.nih.gov>
Subject: Interview request/chlorcyclizine pricing: BuzzFeed News

Hello, NIDDK received an interview request from a Buzzfeed reporter asking about NIH involvement in licensing and drug pricing for chlorcyclizine. Chuck Niebylski, director of NIDDK's Technology Advancement Office, asked that I refer this request to NIH OD as it involves NIH's policy on drug pricing.

Below is the complete email exchange I've had with the reporter, Dan Vergano, and attached is a PDF of an email chain between NIH employees that the reporter received via a public interest group called [Knowledge Ecology International](#), which obtained the records via a FOIA request. (Please note, for background: KEI also [published this 2015 post](#) about the same drug.)

Is NIH OD able to respond to this request?

Thank you,
January W. Payne
Office of Communications and Public Liaison
National Institute of Diabetes and Digestive and Kidney Diseases
NATIONAL INSTITUTES OF HEALTH
Direct 301-435-8115
Cell [redacted] b6
Office 301-496-3583
www.niddk.nih.gov

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From: Dan Vergano [<mailto:dan.vergano@buzzfeed.com>]
Sent: Monday, October 24, 2016 12:29 PM
To: Payne, January (NIH/NIDDK) [E] <january.payne@nih.gov>
Subject: Re: BuzzFeed News: press contact / licensing

January,

Thanks for getting back to me

-- The drug is chlorcyclizine (link to license ann't below), and the public interest group, Knowledge Ecology International (which often looks at NIH licenses) is complaining that its request for "reasonable pricing" requirements in the license were brushed aside to the detriment of taxpayers. The group has just received a public records request (a portion is attached) and suggests they show that NIH is worried more about scaring off the licensee than benefiting the taxpayers

who funded this drug and have no assurance they won't have to pay excessively high prices for it.

-- I'm looking for an agency response to this contention.

-- My deadline is 10/28/16 at 5 PM EDT

-- My questions would basically be:

How do you respond to their complaint?

What are the institute's priorities when licensing these drugs?

How much progress has this licensee made on marketing this drug?

What were the results of the Phase 1 trial that NIH funded on this drug?

Some observers are asking: why grant an exclusive license to a small, unknown company with no track record of bringing drugs to market?

I'd have follow-ups depending on the answers, natch, and would want to hear any responses to smarter questions on all this that your folks might have.

Any help appreciated,

Dan Vergano
BuzzFeed News

b6

Dan Vergano | Science Reporter (DC) [REDACTED] b6
BuzzFeed
1630 Connecticut Ave. 7th Floor, Washington DC 20009

link: <https://s3.amazonaws.com/public-inspection.federalregister.gov/2015-06974.pdf>

Dan Vergano | Science Reporter (DC) [REDACTED] b6
BuzzFeed
1630 Connecticut Ave. 7th Floor, Washington DC 20009

On Mon, Oct 24, 2016 at 11:57 AM, Payne, January
(NIH/NIDDK) [E] <january.payne@nih.gov> wrote:

Dear Dan,

Thanks for your message. Can you please provide more information so I can look into your request?

- What is the drug name, and can you please briefly describe the issue that has been raised? Also, what is the name of the public interest group?
- What is your hard deadline?

- Can you please provide a few examples of questions you'd like to ask?

Best,

January W. Payne

Office of Communications and Public Liaison
National Institute of Diabetes and Digestive and Kidney Diseases

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From: Dan Vergano [mailto:dan.vergano@buzzfeed.com]
Sent: Monday, October 24, 2016 11:25 AM
To: NIDDK NIDDKMEDIA (NIH/NIDDK) <niddkmedia@niddk.nih.gov>
Subject: Fwd: BuzzFeed News: press contact / licensing

Krysten's email responder suggested I send this note to this contact. I have also left a phone message with the press office. I am looking for comment this week.

Ms. Carrera,

I'm a science reporter at BuzzFeed News. I'm looking for a press contact at NIDDK who can address a drug licensing issue at your institute. A public interest group is raising questions about one of your licenses and I'd like to get a response from the institute.

Thanks for any help,

Dan Vergano

BuzzFeed News

b6

Dan Vergano | Science Reporter (DC) | b6
BuzzFeed
1630 Connecticut Ave. 7th Floor, Washington DC 20009

JANUARY PAYNE

@ National Institutes of Health

[National Institutes of Health | 9000 Rockville Pike, Bethesda, MD 20892, USA](#) | Official website of the National Ins (NIH). NIH is one of the world's foremost medical research centers. An agency of...



January Payne on LinkedIn



@NIH | 663K followers | 6K tweets · 3 hours ago

There's still time to submit your @NIH_LRP application! Get started on yours today. Deadline is Nov. 15 bit.ly/2e #studentdebt



[Search for January Payne on Google](#)

Dan is using Senders. [View / edit your own Card](#)

<Reasonable Pricing - Virotas NIH .pdf>

<image001.jpg>

<image001.jpg>

From: Lambert, Richard (NIH/NIAID) [C] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=9668E9326D084AC893665B084FD4FE-LAMBERTR]
Sent: 5/16/2019 12:00:52 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
Subject: FW: [Ip-health] The IPWATCHDOG debate on Bayh-Dole March-In rights

FYI

Richard A. Lambert
Contractor
National Institute of Allergy and Infectious Diseases
National Institutes of Health
U.S. Department of Health and Human Services
5601 Fishers Lane, Rm. 2G47, MSC 9804
Bethesda, MD 20892-9804
(Courier: Rockville, MD. 20852)
301.496.2644 main officeline
240.627.3706 direct line
FAX 240.627.3117
lambertr@niaid.nih.gov

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-----Original Message-----

From: James Love <james.love@keionline.org>
Sent: Thursday, May 16, 2019 7:56 AM
To: Ip-health <ip-health@lists.keionline.org>
Subject: [Ip-health] The IPWATCHDOG debate on Bayh-Dole March-In rights

On May 12, IPWATCHDOG.Com published an article from Frederick Reinhart, a former president of AUTM, the University technology transfer managers' association, claiming a letter by KEI, Health GAP; Housing Works; Doctors Without Borders USA; Public Citizen; Social Security Works; The Institute for Agriculture and Trade Policy; Union for Affordable Cancer Treatment; UNITE HERE; Universities Allied for Essential Medicines; and Yale Global Health Justice Partnership, "misleads on March-in Rights." This was in the context of comments on the NIST Green Paper on the Bayh-Dole Act.

Reinhart's blog quoted unpublished data from another former AUTM president, Ashley Stevens, to support his claims. A third AUTM President, John Fraser, who lists "Entrepreneur in Resident" at NIST on his linkedin page, chimed in on the comments section, making similar criticisms. The Reinhart blog is here:

<https://www.ipwatchdog.com/2019/05/12/knowledge-ecology-international-letter-misleads-march-rights/id=109152/>

I asked IPWATCHDOG if I could respond on their platform, and they graciously agreed. In my 1700 word response, I primarily focused on two of the central arguments that Reinhart, Stevens, Frazer and other like minded critics of march-in rights frequently offer: (1) the claim that public sector investments in products are trivial, relative to private sector investments on products, and (2) that the NIH's 1989 to 1995 experience with the fair pricing clause in CRADAs was evidence against using march-in rights to address excessive prices.

This was my response:

<https://www.ipwatchdog.com/2019/05/15/jamie-love-responds-criticism-knowledge-ecology-international-letter/id=109239/>

Jamie Love Responds to Criticism of Knowledge Ecology International Letter

By James Love

May 15, 2019

"Reinhart and AUTM are arguing that 'available to the public on reasonable terms' does not mean the price has to be reasonable. We disagree, and so do many others."

On May 12, Frederick Reinhart published an article titled “Knowledge Ecology International Letter Misleads on March-In Rights.”

Reinhart is a past president of the Association of University Technology Managers (AUTM), and his views echo those expressed by many in the university technology transfer field, including a frustration that not everyone acknowledges and appreciates the considerable investments and risks undertaken by the for-profit companies that license patents to inventions funded by the federal government.

Knowledge Ecology International (KEI) recognizes the importance of the private sector in bringing therapies to the market, even when federal funding of R&D has played a role, and also that robust returns on those investments have a positive impact on innovation.

I was surprised and disappointed, however, at the way that Reinhart deliberately downplays the importance of the public sector investments.

Reinhart dismisses the federal government’s contribution to the development of enzalutamide (sold by Astellas as Xtandi), by claiming that “less than

\$2 million in federal money was invested in related early work at UCLA,”

which he compared to \$900 million by “companies like Astellas that developed it,” citing Ashley Stevens’ unpublished data.

The original 2016 march-in petition on Xtandi did provide a fairly detailed account of both public and private sector investments in Xtandi. The \$900 million figure cited by Reinhart was certainly not accurate regarding the investments to obtain the initial 2012 registration of the drug.

The 2012 Food and Drug Administration (FDA) medical review relied upon evidence from clinical trials involving only 1,426 patients. The 2016 march-in petition noted that “the two earliest trials (NCT00510718,

NCT01091103) received subsidies from the National Cancer Institute and Department of Defense, in addition to funding from the Prostate Cancer Foundation and other non-profit institutions.” You can take anyone’s estimates of per patient trial costs you like, ignore the federal and charity funding received, and you still don’t get close to the \$900 million Reinhart cites.

Reinhart Undervalues Public Investment

But more important is Reinhart’s undervaluing the public’s investment. The public’s investments in enzalutamide also involved risks. Not every Department of Defense (DOD) or National Institutes of Health (NIH) grant results in a successful product. Joseph DiMasi, in his 2016 paper (which Reinhart cites with approval), got to an estimate of \$2.6 billion in R&D costs by including \$1.1 billion for pre-clinical costs. Both the \$2.6 billion and the \$1.1 billion are of course adjusted for risks of failures and capital costs. However, take note of what Reinhart and his AUTM colleagues are doing. The private sector investments are adjusted for risks and capital costs, but the federal government investments are not. One could make the case that the DOD and NIH investments in preclinical work, including the patented invention, were worth \$1.1 billion, once risks are taken into account. In fact, how much did UCLA sell the patent rights for?

That would be \$1.14 billion, to Royalty Pharma.

In his blog post, Reinhart also writes that the number of NIH Cooperative Research and Development Agreements (CRADAs) executed dropped off when a reasonable pricing clause was introduced, and “increased significantly and quickly” when the clause was eliminated. This claim, made frequently by the technology transfer community, bears some scrutiny. KEI obtained data from the NIH on CRADAs under the Freedom of Information Act (FOIA), which is available here. Until 1996, the NIH only reported what are now called “Standard” CRADAs. Beginning in 1996, the NIH added a new category, “Materials” CRADAs. All of the CRADAs involving the reasonable pricing clause were standard CRADAs.

From 1990 to 1994, the calendar years when the reasonable pricing clause was used for the whole year, the average number of standard CRADAs executed was 33. There was also a significant biotech stock market crash in 1992 and 1993. From 1996 to 2000, the number of standard CRADAs increased, to an average of 46 per year. But a lot was happening that had nothing to do with the reasonable pricing clause.

The average NIH budget was 55% higher in 1996 to 2000 than in 1990 to 1994.

Probably more consequential, from year end 1992 to year end 1994, the NASDAQ biotech index declined from 170.64 to 81.54, a decline of 48%, whereas from year end 1995 to year end 2000, the same index increased from 133.77 to 634.32, an increase of 374%.

More significantly, regarding the CRADA data, the number of standard CRADAs fell to 28 by 2005, and was relatively flat from 2000 to 2013, despite a massive 17-fold increase in the NASDAQ biotech index, and a 64% increase in the NIH budget. Are we supposed to conclude that increases in the NIH budget or rising share prices and new private investments aren’t good for innovation because the number of CRADAs did not increase from 2000 to 2013?

What Is the NIST Green Paper Really About, and Why is AUTM Unhappy with KEI?

What is at issue in the NIST Green Paper are the safeguards in the Bayh-Dole Act designed to protect the public from “unreasonable use of inventions.” This is not just KEI’s rhetoric, it’s a quote from 35 USC § 200, the policy and objective of the Bayh-Dole Act.

when the Bayh-Dole Act was passed in 1980, it had several public safeguards. One safeguard was a five-year limit on exclusive rights for federally-funded patents held by universities and small businesses. The five-year limit was subject to possible extensions, based upon a compelling need. That safeguard was eliminated in 1984, in P.L. 98-620. The 1980 Act also reserved for the federal government a royalty-free right to use patented inventions it funded anywhere in the world, and to exercise march-in rights. The 1980 Act also limited the secrecy of government patent licenses and required a minimum of 60 days' notice before granting an exclusive license. Later, that provision on secrecy was amended, making licensing more secret, and the public comment period was reduced from 60 to 15 days.

Reinhart is focusing on the march-in right, and in particular, the question of whether pricing can be addressed as an abuse or factor in granting a march-in. It should be noted that Senator Bayh himself, in a March 3, 1997 letter to then-HHS Secretary Donna Shalala, proposed regulations on licensing to protect consumers from unreasonably high prices for medical care in the Cellpro case, when he represented Cellpro. Later, when Bayh was a lobbyist and Dole was a Pfizer spokesman for Viagra, they made claims about the legislative intent of the Bayh-Dole Act, but what we know for sure is that the act defines "practical application" of an invention to include an obligation to make the benefits of the invention "available to the public on reasonable terms."

Reinhart and AUTM are arguing that "available to the public on reasonable terms" does not mean the price has to be reasonable. We disagree, and so do many others, including, recently, Professor John Thomas in an April 18, 2019 Washington Post report on the NIST Green Paper.

AUTM and others have asked NIST to change the regulations for the Bayh-Dole Act so that march-in rights can never be used when prices are the issue.

This brings us back to the Xtandi case. In July 2017, the Senate Armed Services Committee issued the following directive to the Department of Defense (a funder of the Xtandi Orange Book patents).

Licensing of federally owned medical inventions

The committee directs the Department of Defense (DOD) to exercise its rights under sections 209(d)(1) or 203 of title 35, United States Code, to authorize third parties to use inventions that benefited from DOD funding whenever the price of a drug, vaccine, or other medical technology is higher in the United States than the median price charged in the seven largest economies that have a per capita income at least half the per capita income of the United States.

115TH Congress, 1st Session, 2017, Senate Report 115-125. National Defense Authorization Act for Fiscal Year 2018. Report to accompany S. 1519, on page 173. July 10, 2017.

Subsequently, my brother, Clare Love, an Army veteran of the Vietnam War and a prostate cancer patient, and Dr. David Reed, another prostate cancer patient, asked DOD to enforce the directive, in the case of Xtandi. The petition stated:

The price of Xtandi in the United States is more than four times the median price in the seven high income countries identified by the U.S. Senate Armed Services Committee in 2017 to be used to determine if the U.S. price on a Department of Defense (DoD)-funded drug is reasonable. The price in the U.S. is five times the reimbursed price in Japan, where Astellas is headquartered. The failure by Astellas to make the drug available to the public on reasonable terms can and should be remedied by the U.S. government through exercising the federal government's royalty-free or march-in rights in the patents.

This is a very expensive drug, for a very common type of cancer. In January 2018, the average wholesale price of Xtandi was \$159,215.80 per year (four capsules per day dose) for the treatment of prostate cancer.

This is what Reinhart is fighting for: the right of a large Japanese drug company to charge U.S. prostate cancer patients five times as much as the list price in Japan, for a drug invented with grants from the NIH and the U.S. Army.

For KEI, the fact that the government has failed to enforce the obligation to make inventions "available to the public on reasonable terms" is the definition of insanity, not (as suggested in the comments by former AUTM president John Fraser in the Reinhart blog post), KEI's continued insistence that this obligation be honored.

--

James Love. Knowledge Ecology International U.S. Mobile +1.202.361.3040 U.S. office phone
+1.202.332.2670 <http://www.keionline.org> <<http://www.keionline.org/donate.html>>
twitter.com/jamie_love

Ip-health mailing list
Ip-health@lists.keionline.org
http://lists.keionline.org/mailman/listinfo/ip-health_lists.keionline.org

From: Jambou, Robert (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=FF42A9FA39824980AA9E36AF49E56CBC-JAMBOUR]
Sent: 7/23/2018 8:35:26 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718ccb29fab-rohrbaum]
Subject: RE: KEI [Goldman] FOIA #45260

b5

Bob J.

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Monday, July 23, 2018 4:32 PM
To: Jambou, Robert (NIH/OD) [E] <jambour@od.nih.gov>
Subject: RE: KEI [Goldman] FOIA #45260

b5

From: Jambou, Robert (NIH/OD) [E]
Sent: Monday, July 23, 2018 4:07 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Subject: RE: KEI [Goldman] FOIA #45260

b5

Let me know if this poses a problem and I will consult with the NIH FOIA officer in this regard (with approval from senior staff) if necessary.

Bob J.

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Monday, July 23, 2018 3:27 PM
To: Jambou, Robert (NIH/OD) [E] <jambour@od.nih.gov>
Subject: RE: KEI [Goldman] FOIA #45260

b5

From: Jambou, Robert (NIH/OD) [E]
Sent: Monday, July 23, 2018 2:48 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Subject: RE: KEI [Goldman] FOIA #45260

b5

Bob J.

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Monday, July 23, 2018 2:41 PM
To: Jambou, Robert (NIH/OD) [E] <jambour@od.nih.gov>
Subject: RE: KEI [Goldman] FOIA #45260

Just wondered.

b5

From: Jambou, Robert (NIH/OD) [E]
Sent: Monday, July 23, 2018 2:39 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Subject: RE: KEI [Goldman] FOIA #45260

Typically not (and not if they are NIH employees). I cannot recall ever doing that.
Is there something specific?

Bob J.

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Monday, July 23, 2018 2:35 PM
To: Jambou, Robert (NIH/OD) [E] <jambour@od.nih.gov>
Subject: RE: KEI [Goldman] FOIA #45260

For released emails, would you redact names of people sending, receiving emails?

From: Jambou, Robert (NIH/OD) [E]
Sent: Monday, July 23, 2018 12:49 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Subject: RE: KEI [Goldman] FOIA #45260

Done – I added the incoming request to the TTIP FOIA folder – see page 2 (blue highlight).

Bob J.

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Monday, July 23, 2018 12:36 PM
To: Jambou, Robert (NIH/OD) [E] <jambour@od.nih.gov>
Subject: RE: KEI [Goldman] FOIA #45260

Will do. Can you remind me what the request was exactly?

From: Jambou, Robert (NIH/OD) [E]
Sent: Monday, July 23, 2018 12:32 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Subject: KEI [Goldman] FOIA #45260

Hi Mark,

I have finished the review of the KEI March-In Petition FOIA.
There are 322* responsive .pdf files (including attachments) for your QC review.

To facilitate the task, I have divided the responsive categories into 3 types:

b5

If you could take a look at these files, I would appreciate it (especially the ones labeled "Check or muCheck". If you have comments, please use the Adobe comment tool and add your initials to the end of the file so I can spot those quickly.

I have created a folder and copied the responsive files here into three different sub-folders according to status: [C:/TIP/KEI_Goldman_FOIA_45260](file:///C:/TIP/KEI_Goldman_FOIA_45260)

Happy to help you with this. Let me know

b5

Regards,

REL0000024446

Bob J.

From: Koniges, Ursula (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=D5AE2C3139654BC0B9B95718D516310B-KONIGESUM]
Sent: 1/10/2019 9:19:22 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718ccb29fab-rohrbaum]
Subject: RE: Drug Pricing & Secretary Azar
Attachments: Drug Pricing - UK.docx

Hi Mark,

I've gotten the

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b5

What do you think of these changes (attached)? Please feel free to further edit/develop.

Thanks,
-Ursula

From: Koniges, Ursula (NIH/OD) [E]
Sent: Thursday, January 10, 2019 4:09 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>
Subject: RE: Drug Pricing & Secretary Azar

I've added the following bullet to the

b5

b5

From: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Sent: Thursday, January 10, 2019 4:07 PM
To: Koniges, Ursula (NIH/OD) [E] <ursula.koniges@nih.gov>
Subject: RE: Drug Pricing & Secretary Azar

I would put it in the

b5

b5

From: Koniges, Ursula (NIH/OD) [E] <ursula.koniges@nih.gov>
Sent: Thursday, January 10, 2019 4:01 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Subject: Drug Pricing & Secretary Azar

Hi Mark, quick FYI that

b5

Azar Says He And Trump Are Determined To Reduce Prescription Drug Prices.

On Fox Business' Varney & Co. (1/9, 198K), HHS Secretary Alex Azar was interviewed about the fact that manufacturers recently raised prescription drug prices, hindering President Trump's efforts to lower them. Azar said, "I want to be really clear to pharma companies out there and to pharmacy benefit managers: the President and I will not stop until list prices of drugs come down. This behavior has to stop, drug prices must come down and we will roll out more regulatory and legislative proposals and we will work

with Democrats and Republicans to get drug prices down." Asked about criticism that the President is attempting to institute drug price controls, Azar stated, "The companies that increased their prices...on January 1 all admitted they were doing so basically to funnel kickbacks in the form of rebates to pharmacy benefit managers to keep preferred status of their drugs on the formularies available to patients. Now we've seen some good behavior: you know Amgen, Merck, Gilead, each of them have products" whose list prices "they have significantly reduced." Azar said, "We need to see more of this, we need other companies to follow, we need bigger products to have those price decreases." [Fox Business](#) (1/9, Limitone, 1.55M) also reports on the interview.

In Tweets, Azar Demands That Manufacturers Lower Prescription Drug Prices.

[BioPharma Dive](#) (1/9, Dunn) reports that drugmakers "largely reverted to boosting list prices in January even after a year of criticism from the Trump administration and some companies pledging to hold off. The White House is now weighing in with Health and Human Services Secretary Alex Azar threatening further regulatory and legislative action if list prices do not come down." On Wednesday, "Azar put the industry and pharmaceutical benefit managers, or PBMs, on blast with a tweet thread...capped off with a cable news hit." [Health Exec](#) (1/9, Baxter) reports that Azar tweeted, "Prices must start coming down." But "the message – which was published a day after Trump called a meeting with White House officials on the issue – didn't come with any new proposals or plans from the agency he leads. The Twitter action also comes a day before Democrats in Congress plan to introduce a legislative package to 'drastically' reduce drug prices."

Columnist: Azar's Tweets Show Trump Administration Is Not Happy With Drug Price Hikes.

Max Nisen writes in a [Bloomberg View](#) (1/9, 5.74M) column that after raising prices on January 1, "drug executives followed up this week with less-than-contrite messaging at" the J.P. Morgan Chase & Co. Healthcare Conference, "signaling the industry's reluctance to change in the face of constant criticism." Nisen says the Trump Administration is displeased with the price increases. On Tuesday, President Trump "reportedly summoned advisers to meet on the issue, and on Wednesday, Health and Human Services Secretary Alex Azar launched a tweet storm to take the sector [to task] for its lack of progress."

b5

b5

b5

b5

b5

From: Joe Allen [jallen@allen-assoc.com]
Sent: 7/11/2017 5:10:29 PM
To: Hammersla, Ann (NIH/OD) [/O=NIH/OU=NIHEXCHANGE/cn=Recipients/cn=hammerslaa]; Rohrbaugh, Mark (NIH/OD) [/O=NIH/OU=NIHEXCHANGE/cn=OD/cn=ROHRBAUM]
Subject: My take on the King amendment
Attachments: Senator King's amendment is bad law and bad policy.docx

Prepared this for a client which gave me permissions to share it with a few key stakeholders

>>>

Senator King's Amendment Is Bad Law and Bad Policy

Summary

Senator Angus King successfully added an amendment to the National Defense Authorization Act during the mark up by the Senate Armed Services Committee directing the Department of Defense to use two provisions of the Bayh-Dole Act (P.L. 96-517, as amended) to issue compulsory licenses for any drug developed from DOD funding which is priced "higher in the United States than the median price charged in the seven largest economies that have a per capita income at least half the per capita income of the United States."

The problem with the amendment is that it's based on a long discredited theory of how the law operates which was repeatedly rejected by the National Institutes of Health, and most recently by the Department of Defense.

The King amendment is the latest attempt by a determined band of critics (led by Ralph Nader acolyte Jamie Love's organization Knowledge Ecology International) to overturn these well grounded rulings, providing Love with a powerful weapon to bludgeon drug developers. If passed, the amendment will inflict considerable damage to a system that helps drive the U.S. economy by undermining public/private sector R&D partnerships. Ironically, one result would be that fewer new drugs would be developed to protect public health. The amendment could also doom the Department of the Army's effort to develop a much needed Zika vaccine based on a Walter Reed Medical Center invention.

Background

The purpose of the Bayh-Dole Act is to encourage the commercial development of federally funded inventions by decentralizing the ownership and management of inventions from Washington to universities and small companies making them under government grants and contracts. The law also allows federal laboratories to license the inventions they discover.

Before Bayh-Dole, the government took ownership of such inventions, offering them to any and all under non-exclusive licenses. *The Comptroller General found that not a single new drug had been developed as a result.* A key objective of the law was creating a uniform patent policy across all agencies, replacing more than 20 inconsistent policies then in place.

Since passage of the law in 1980, more than 200 new drugs and vaccines are on the market based on federally funded inventions, and more than 2 new start-up companies and new products are produced every day. A new BIO/Association of University Technology Managers study found that in 20 years (1996- 2015) the law made a **\$1.33 trillion** contribution to the U.S. economy while supporting more than **4 million** good paying jobs. No other country comes close to matching these numbers. The Economist Technology Quarterly said: "*Possibly the most inspired piece of legislation to be enacted in America over the past half century was the Bayh-Dole Act of 1980... More than anything, this simple policy helped to reverse America's precipitous slide into industrial irrelevance.*"

The King amendment puts this at risk.

When passing Bayh-Dole, Congress was concerned that dominant companies might license breakthrough inventions to suppress them if they competed with existing products, so a "march-in" provision was adopted. If it's determined that good faith efforts are not being made to bring an invention to "practical application" so that it is "available to the public on reasonable terms" the funding agency can insist that additional licenses are issued so the invention can be commercialized. In the context of the times "reasonable terms" meant that the company was really trying to sell the product to the public. March-ins can also be used if health or other national emergencies arise and the licensee is unable to manufacture enough product to meet public needs.

The law gives agencies a royalty free license to use inventions they fund to meet government mission needs. It is the march in and government use authorities which the King amendment addresses.

Twenty years after Bayh-Dole was enacted, two professors "discovered" a new meaning in the law. Their op-ed in the Washington Post "Paying Twice for the Same Drugs" claimed that available on "reasonable terms" meant the government could issue compulsory licenses whenever it didn't like a product's price. Senators Bayh and Dole immediately replied that this was a gross misinterpretation of their law as there was no reference to how a product was priced in the statute or the legislative history, which would have been provided if that was their intent. They stated that their law only gives agencies the authority to march-in if a product wasn't available for public use.

Ignoring this rebuttal, critics of the law filed a march-in petition at the National Institutes of Health against the AIDS drug Norvir because of its price. Senator

Bayh testified at the ensuing NIH public meeting that the language of the petition deliberately misquoted the legislative history of Bayh-Dole, adding that if Congress wants the law to control prices for successfully commercialized products it must amend the statute and define what a "reasonable price" means. That has never been done.

The King amendment doesn't amend the statute as required; it simply directs DOD to exercise a march-in authority which the law doesn't provide. If enacted, this will cause chaos.

The King amendment is directed at two targets: attempts by the critics to force compulsory licenses for Xtandi, a prostate cancer drug arising from NIH and Dept of the Army funding; and opposition to a pending exclusive licensing agreement between the Army and Sanofi to develop a Zika vaccine based on a Walter Reed Medical Center invention.

Xtandi

Last June, NIH Director Francis Collins and then HHS Secretary Sylvia Burwell dismissed Jamie Love's march in petition against Xtandi. Love argued that because the drug is sold at a higher price in the U.S. than abroad it met the march-in criteria of Bayh-Dole. In his denial letter, Dr. Collins directly rebutted Love's contention that price, not market availability, is a march in trigger, citing Love's own data:

"... Xtandi is broadly available as a prescription drug. Your letter states that sales of enzalutamide increased 77% from Fiscal Year 2013 to Fiscal Year 2014..., however, it provides no information and no information was identified from public sources that enzalutamide is currently or will be in short supply. In view of the above information presented in your letter and your follow-up correspondence and public information identified by the NIH, we decline to proceed with the government's march-in authorities at this time or utilize the government's license to the patents."

Love also filed a march-in petition at the Department of Defense, which was denied. It is that determination which the King amendment seeks to overrule.

This was the *fifth time* (two march in petitions against Norvir, one against Latanoprost, a glaucoma drug, and two against Xtandi) that those behind the King amendment had filed march-in petitions based on the price of a successfully commercialized drug-- all of which were appropriately dismissed as not falling

under the criteria of the Bayh-Dole Act. Regardless, Love refiled his petition against Xtandi with NIH earlier this year.

Zika vaccine

Because of the urgency in developing an effective vaccine to combat Zika, the Dept of the Army posted a Federal Register notice, as required by Bayh-Dole, that it was seeking a licensee for a Walter Reed Medical Center invention. Due to the high risks involved, the Army offered to combine the license with a "Cooperative R&D Agreement" (CRADA) under which the Department would underwrite the necessary clinical trials. Only one company, Sanofi, applied.

The critics immediately began a media campaign joined by prominent Democrats like Sen. Bernie Sanders objecting to the exclusive license to Sanofi and demanding that the Army include price control language in any deal in light of the government's funding of the project. Sanofi responded that it could not accept such language.

The King amendment is aimed at forcing a price control formula into the agreement over the objections of the Army and Sanofi. *Ironically, the end result could be that Sanofi walks away, so rather than lowering costs, the vaccine would remain on the shelf.*

Similar Congressional pressure was applied in the 90's forcing NIH to include a "reasonable pricing" provision for its CRADAS. Rather than lowering prices, the provision led to a collapse of NIH/industry partnerships. Five years later, then NIH Director Harold Varmus revoked the provision explaining: *"the pricing clause has driven industry away from potentially beneficial scientific collaborations with [NIH] scientists without providing an offsetting benefit to the public."*

Two years after Dr. Varmus intervened, NIH/industry CRADAS were up more than 500%. Since that experience, NIH has been adamantly opposed to including "reasonable pricing" provisions in its licenses or CRADAS, seeing them as counterproductive to the need to effectively develop new drugs to meet patient needs.

If enacted, the King amendment would have the same disastrous results at the Department of Defense as the previous attempt inflicted on.NIH.

The King Amendment Could Harm Military Patients

One situation did meet the statutory criteria of the march in provision. Several years ago Genzyme was forced to halt production of an orphan drug, Fabrazyme, because of quality control issues. Love's organization filed a march in petition with NIH, which had funded the research leading to the invention. After closely investigating the situation, NIH determined that issuing licenses to new companies would delay availability of the drug as it would require longer for them to obtain needed FDA clearances and get in production than it would take Genzyme to get its plant back on-line. Shortly thereafter, Genzyme was back in operation and the crisis passed.

Because the King amendment only focuses on price, not availability, it forces DOD to issue compulsory licenses rather than buying from the drug developer under its convoluted formula. That could inflict unnecessary suffering on patients at military facilities like Walter Reed. As in the situation NIH faced with Fabrazyme, trying to have a new company gain needed regulatory clearances and get into production could mean that a desperately needed drug or vaccine would be seriously delayed for patients in DOD hospitals even though it was readily available in the commercial marketplace. The Department could also find the anticipated savings were illusory as the cost of a production run for an orphan drug solely for a small number of military patients could be very high.

The Impact of the King Amendment on Small Business

Some of the greatest damage of the amendment will fall on small companies, many of which form around academic inventions, forming the backbone of our biotechnology industry. About 70% of university inventions are licensed to small companies. Unlike other countries, about half of the new drugs in the U.S. originate in small businesses.

It's estimated that companies spend \$100 dollars on development for every \$1 the government spent supporting the research leading to a patent. That's not surprising, because federally funded inventions are typically at a very early stage of development, more like ideas than products. Under the Bayh-Dole system, the risks and expenses of commercialization falls on the private sector. In drug development, that's a considerable burden.

Of every 10,000 compounds about 250 make it to preclinical testing, 5 proceed to clinical trials and just 1 enters the marketplace. Of these, only 20% earn a profit

and must pay the expenses for all that died in the pipeline. Developing a new drug is estimated to cost companies between \$800 million to over \$2 billion dollars, requiring more than a decade for development.

What venture capitalist would fund a life science start-up built around a federally funded invention if the King amendment passed? Because of arbitrary foreign price controls placed on drugs sold abroad (the vast majority of which are developed in the United States) after assuming all the risks, *a start-up could see the Dept of Defense forced to grant compulsory licenses to its competitors (including big pharma) under Sen. King's formula.* The U.S. lead in the life sciences would be jeopardized and patients around the world desperately hoping for relief would be the losers as many might see developing new drugs as simply no longer worth the effort.

Finally, the King amendment requires the Department of Defense to apply the Bayh-Dole Act inconsistently with every other agency, thus destroying the Congressional goal of having a uniform government patent policy.

It's clear that the King amendment is bad law-- and bad policy.

From: Hammersla, Ann (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=87FB28AA23744C0B855EF0683AC2E8B4-HAMMERSLAA]
Sent: 4/20/2018 11:42:05 AM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718ccb29fab-rohrbaum]
Subject: FW: Response Letter from NIH
Attachments: Robert F. Firestone letter-U of Penn-KEI-Juxtapid 4.19.2018.pdf; 1a 2018-03-28 Penn Response to NIH re KEI Allegations-Rader-Executed.pdf

FYI - Ann

From: Jackson, Stephanie (NIH/OD) [C]
Sent: Thursday, April 19, 2018 4:40 PM
To: Robert.firestone@ogc.upenn.edu
Cc: Bulls, Michelle G. (NIH/OD) [E] <michelle.bulls@nih.gov>; Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>
Subject: Response Letter from NIH

Sent on behalf of Michelle G. Bulls –

Good afternoon Mr. Firestone,

Attached please find, letter from the NIH in response to your letter dated March 28, 2018.

Thank you,
MGB

Stephanie G. Jackson, Executive Assistant
Contractor- Ripple Effect Communications, Inc.
Office of Policy for Extramural Research Administration, OER
NIH Office of the Director

6705 Rockledge Drive, Suite 350A
Bethesda, MD 20892-7974
Phone: 301-451-4221
Email: Stephanie.jackson3@nih.gov



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
Bethesda, Maryland 20892

April 19, 2018

Robert F. Firestone, Esq.
Associate General Counsel
University of Pennsylvania
Office of General Counsel
2929 Walnut Street, Suite 400
Philadelphia, Pennsylvania 19104-5099

Sent by Email: Robert.firestone@ogc.upenn.edu

Dear Mr. Firestone:

Thank you for your letter of March 28, 2018 providing information about the National Institutes of Health (NIH) support of four M01 awards made to the University of Pennsylvania (University). Your information was provided in response to Knowledge Ecology International's (KEI) March 19, 2018 correspondence and supporting information to NIH concerning certain University licensed patents that KEI asserts failed to disclose federal government support. KEI also recommends that the federal government take title to the invention(s) based on its findings that the University failed to comply with the Bayh-Dole Act.

Your correspondence indicates that it is the University's position that it was not required to disclose the inventions leading to the issued patents to NIH for INN lomitapide because the dosing methods were not conceived or first reduced to practice using federal funds. The Phase I/II clinical trials for the dosing methods were funded solely by the Doris Duke Charitable Foundation.

The NIH is in the process of reviewing KEI's request, the federal government's support of the University's inventor, Dr. Daniel Rader, and his research supported by the NIH M01 awards and all other NIH awards made to the University for Dr. Rader's research.

As requested, if the NIH requires additional information from the University, we will contact you directly. At the conclusion of the NIH's review the University will be provided with NIH's review and determination.

Sincerely,

b6

Michelle G. Bulls *J*
Director
Office of Policy for Extramural Research Administration
Office of Extramural Research
National Institutes of Health

b4

b4

From: Greene, Jaime (NIH/NCI) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=E06E39F0BCD34511A92DF20C5DC8722A-GREENEJAIME]
Sent: 12/18/2018 4:24:05 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
CC: Rodriguez, Richard (NIH/NCI) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=8092cb5394e04733ac0d4d84d25f65e5-rodrigr]
Subject: RE: Comments on "Prospective Grant of an Exclusive Patent License: Agonist/Antagonist Compositions and Methods of Use for certain inventions" (83 FR 61659)

Dear Mark,

See below KEI's comments in response to my recent Federal Register notice. Since KEI did not ask any questions, NCI has no plans to respond.

Please let me know if you have any questions.

Thanks,

Jaime

Jaime Meredith Greene, M.S.
Senior Technology Transfer Manager
NCI Technology Transfer Center

Note: This email may contain confidential information. If you are not the intended recipient, any disclosure, copying or use of this email or the information enclosed therein is strictly prohibited, and you should notify the sender for return of any attached documents

From: James Love <james.love@keionline.org>
Sent: Sunday, December 16, 2018 1:11 PM
To: Greene, Jaime (NIH/NCI) [E] <greenajaime@mail.nih.gov>
Cc: Claire Cassedy <claire.cassedy@keionline.org>
Subject: Comments on "Prospective Grant of an Exclusive Patent License: Agonist/Antagonist Compositions and Methods of Use for certain inventions" (83 FR 61659)

Jaime M. Greene
Senior Licensing and Patenting Manager
NCI Technology Transfer Center
9609 Medical Center Drive, RM 1E530 MSC 9702
Bethesda, MD 20892-9702
Rockville, MD 20850-9702
Telephone: (240) 276-5530
Facsimile: (240) 276-5504
Email: greenajaime@mail.nih.gov

December 16, 2018

Re: Comments on "Prospective Grant of an Exclusive Patent License: Agonist/Antagonist Compositions and Methods of Use for certain inventions" (83 FR 61659)

Dear Jaime Greene,

We are writing to provide comments on the Prospective Grant of an Exclusive Patent License: Agonist/Antagonist Compositions and Methods of Use for certain inventions to Bull Run Capital, Inc. located in Vancouver, BC, Canada, as noticed in the Federal Register, 83 FR 61659.

According to the notice, the “prospective exclusive license territory may be worldwide and the field of use may be limited to: “Use of the TRPV1 antagonists BCTC, AMG9810, JYL-827, Capsazepine or IodoRTX combined with a TRPV1 agonist in a composition for the temporary incapacitation of a subject,” ” for “novel compositions comprising a transient receptor potential cation channel subfamily V member 1 (TRPV1) receptor agonist and an antagonist in certain ratios which allow for the onset of agonist action followed by alleviation by antagonist action, and methods of use in personal defense and law enforcement.”

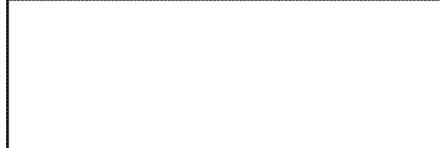
The relevant patents and patent applications include:

1. U.S. Provisional Patent Application No. 61/340,063, filed March 12, 2018, now abandoned, titled “Agonist/Antagonist Compositions and Methods of Use”, HHS Ref. No.: E-048-2010-0-US-01;
2. PCT Patent Application Serial No. PCT/US2011/028132, filed March 11, 2011, now abandoned, HHS Reference Number E-048-2010-0-PCT-02 titled “Agonist/antagonist compositions and methods of use”;
3. U.S. Patent 9,277,748 (Application No. 13/634,447) filed March 11, 2011, issued March 8, 2016, titled “Agonist/antagonist compositions and methods of use”, HHS Ref. No.: E-048-2010-0-US-04;
4. Canada Patent Application Serial No. 2,792,878, filed March 11, 2011, HHS Reference Number E-048-2010-0-CA-03 titled “Agonist/antagonist compositions and methods of use”; and
5. U.S. Patent Application Serial No 15/010,830, filed January 29, 2016, HHS Reference Number E-048-2010-0-US-05, titled “Agonist/antagonist compositions and methods of use”.

KEI’s comments are as follows:

1. Improvements in the efficacy and safety of non-lethal weapons for defense are important.
2. The field of use restriction is appropriate. The NIH should explicitly exclude therapeutic products and uses from the field of use, as some capsaicin agents have therapeutic potential.
3. The price of any products based upon the licensed inventions should be available to U.S. law enforcement agencies and U.S. residents at prices no greater than in Canada and other similar countries with per capita incomes at least 50 percent of the U.S.

Sincerely,



James Love
Knowledge Ecology International
1621 Connecticut Avenue, Suite 500
Washington, DC 20009
<http://keionline.org>
james.love@keionline.org

--
James Love. Knowledge Ecology International
<http://www.keionline.org>
twitter.com/jamie_love

From: James Love [jamespackardlove@gmail.com]
Sent: 1/20/2017 12:34:16 AM
To: Rohrbaugh, Mark (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=OD/cn=ROHRBAUM]
CC: Kassilke, Deborah (NIH/OD) [E] [/O=NIH/OU=Nihexchange/cn=od/cn=kassilked]; claire.cassedby@keionline.org
Subject: Re: Your requests for information from NIH OTT

We can't FOIA a database or require records be generated under FOIA. We can FOIA every CRADA, which is what we are going to be forced to do.

But if we knew what records were in the database, a query might save everyone a lot of time.

On Fri, Jan 20, 2017 at 1:07 AM, Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@od.nih.gov> wrote:

There is no "list" but we do have a database with CRADA and license information.

From: James Love [mailto:jamespackardlove@gmail.com]
Sent: Thursday, January 19, 2017 7:01 PM
To: Kassilke, Deborah (NIH/OD) [E] <deborah.kassilke@nih.gov>
Cc: claire.cassedby@keionline.org; Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>
Subject: Re: Your requests for information from NIH OTT

These are the types of data that make it hard to believe you don't have registry or list of the CRADAs.

<https://www.ott.nih.gov/tt-metrics/crada-metrics>

On Fri, Jan 20, 2017 at 12:56 AM, James Love <jamespackardlove@gmail.com> wrote:

Thank you.

We do note that the NIH is able to report the total number of CRADAs in any given year, and also that that number is quite a bit smaller than the number of CRADAs noticed in the federal register.

For number of CRADAs, <https://www.ott.nih.gov/ott-statistics>

We are mostly interested in the Standard CRADAs.

We thought if the NIH could provide a count of the number of CRADAs, they must have a registry or list or database that lists the CRADAs, with the name of the CRADA partner and the purpose of the CRADA.

We were surprised when we were told that no such lists exist.

The CRADAs mentioned in the annual reports do not seem inclusive of all CRADAs in a given year.

For example:

In FY15, NIH Institutes executed 5,826 of these collaboration and transfer agreements, including 101 new Cooperative Research and Development Agreements (CRADAs).

I don't think there are 101 CRADAs listed in the annual report, or even the 73 for Standard CRADAs.

So, while the Annual report is useful and interesting, we still don't know who is getting the standard CRADAs.

Also, does the NIH issue exclusive licenses under the CRADAs that are not noticed in the federal register? We were told that the NIH practice was to not provide public notice and comment on all CRADAs and that public notice and comment is not available for all exclusive licenses from CRADAs.

Jamie

On Fri, Jan 20, 2017 at 12:26 AM, Kassilke, Deborah (NIH/OD) [E] <deborah.kassilke@nih.gov> wrote:

Mr. Love –

Recently your office contact me and two other employees in my office with questions concerning royalty payments, the use of the Federal Registry in tracking NIH CRADAs, and a request for information on the process by which the NIH enters into a CRADA with an industry collaborator. I am aware that Mark Rohrbaugh (cc'd) spoke directly with Claire Cassidy to discuss many of the CRADA related process components including the use of Federal Register notices and how IP is addressed in a CRADA. If you still have questions regarding the use of CRADAs at NIH, we can certainly schedule another call with you.

I confirmed that the NIH FOIA office is still working on a FOIA request for you concerning royalty payment information. They apologize for the delay, but the FOIA office is short staffed at this time and they are working diligently to hire and train new staff. We just last week brought in an Acting Director for the FOIA office, Katherine Uhl, who is on detail to us from the FDA. She is working diligently to keep the plates spinning and asked that I relay to you they are working on the request. Ms. Uhl invites you to contact her office for a status of your FOIA request if you so desire; that number is 301-496-5633.

I hope that you are aware that our annual reports and statistics can be found on our website in the “MEDIA Room” tab; they may be helpful to you.

Please let me know if you would like another call scheduled with Mark and me; we will gladly set something up.

Deb

Deborah Kassilke

Director, Office of Technology Transfer

National Institutes of Health

6011 Executive Boulevard, Suite 325

Rockville, MD 20852

E-Mail: Deborah.Kassilke@nih.gov

Phone: 301-435-5294

Cell:

b6

James Love. US Mobile is +1.202.361.3040. Geneva Mobile is +41.76.413.6584

http://twitter.com/jamie_love, <http://keionline.org/jamie>

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James Love. US Mobile is +1.202.361.3040. Geneva Mobile is +41.76.413.6584

http://twitter.com/jamie_love, <http://keionline.org/jamie>

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James Love. US Mobile is +1.202.361.3040. Geneva Mobile is +41.76.413.6584
http://twitter.com/jamie_love, <http://keionline.org/jamie>

From: Fine, Amanda (NIH/OD) [E] [/O=NIH/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=FINEAB]
Sent: 10/24/2016 7:51:18 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=OD/cn=ROHRBAUM]
Subject: RE: Interview request/chlorcyclizine pricing: BuzzFeed News

Ok thanks! I'll wait to hear from you.

Amanda

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Monday, October 24, 2016 3:49 PM
To: Fine, Amanda (NIH/OD) [E] <amanda.fine@nih.gov>
Subject: Re: Interview request/chlorcyclizine pricing: BuzzFeed News

b5

Sent from my iPhone

On Oct 24, 2016, at 8:28 PM, Fine, Amanda (NIH/OD) [E] <amanda.fine@nih.gov> wrote:

b5

Ideally we'd want a response that is able to answer all of Dan's questions:

What are the institute's priorities when licensing these drugs?
How much progress has this licensee made on marketing this drug?
What were the results of the Phase 1 trial that NIH funded on this drug?
Some observers are asking: why grant an exclusive license to a small, unknown company with no track record of bringing drugs to market?

Thanks Mark! Hope you're not working while on vacation.

Amanda

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Monday, October 24, 2016 3:22 PM

To: Fine, Amanda (NIH/OD) [E] <amanda.fine@nih.gov>
Cc: McBurney, Margaret (NIH/OD) [E] <mmcburney@od.nih.gov>; Hardesty, Rebecca (NIH/OD) [C] <rebecca.hardesty@nih.gov>; Myles, Renate (NIH/OD) [E] <mylesr@od.nih.gov>; Wojtowicz, Emma (NIH/OD) [E] <emma.wojtowicz@nih.gov>
Subject: Re: Interview request/chlorcyclizine pricing: BuzzFeed News

I am available.

b5

b5

Sent from my iPhone

On Oct 24, 2016, at 8:10 PM, Fine, Amanda (NIH/OD) [E] <amanda.fine@nih.gov> wrote:

Greetings-

I'm including all three of you per Mark's out of office and given that the reporter's deadline is October 28.

NIDDK received the below inquiry from Dan Vergano at Buzzfeed regarding Knowledge Ecology International's (KEI) questions about the drug chlorcyclizine which had/has a small trial at the CC. Attached is a back and forth with NIDDK/NCATS that KEI got through FOIA. Dan's questions are below.

b5

b5

Thank you in advance for your input and guidance,
Amanda

Amanda Fine
Deputy, News Media Branch
National Institutes of Health
Tel: 301-496-7246
Email: amanda.fine@nih.gov
Web: <http://www.nih.gov>

NIH . . . Turning Discovery Into Health

From: Payne, January (NIH/NIDDK) [E]
Sent: Monday, October 24, 2016 2:54 PM
To: OCPLPressTeam <OCPLPressTeam@od.nih.gov>; ODOCPL Interviews (NIH/OD OCPL) <ODOCPLInterviews@mail.nih.gov>

Cc: NIDDK NIDDKMEDIA (NIH/NIDDK) <niddkmedia@niddk.nih.gov>
Subject: Interview request/chlorcyclizine pricing: BuzzFeed News

Hello, NIDDK received an interview request from a Buzzfeed reporter asking about NIH involvement in licensing and drug pricing for chlorcyclizine. Chuck Niebylski, director of NIDDK's Technology Advancement Office, asked that I refer this request to NIH OD as it involves NIH's policy on drug pricing.

Below is the complete email exchange I've had with the reporter, Dan Vergano, and attached is a PDF of an email chain between NIH employees that the reporter received via a public interest group called Knowledge Ecology International, which obtained the records via a FOIA request. (Please note, for background: KEI also published this 2015 post about the same drug.)

Is NIH OD able to respond to this request?

Thank you,
January W. Payne
Office of Communications and Public Liaison
National Institute of Diabetes and Digestive and Kidney Diseases
NATIONAL INSTITUTES OF HEALTH
Direct 301-435-8115
Cell [redacted] b6
Office 301-496-3583
www.niddk.nih.gov

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<image001.jpg>

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Watch how medical research saves lives and improves health

From: Dan Vergano [<mailto:dan.vergano@buzzfeed.com>]
Sent: Monday, October 24, 2016 12:29 PM
To: Payne, January (NIH/NIDDK) [E] <january.payne@nih.gov>
Subject: Re: BuzzFeed News: press contact / licensing

January,

Thanks for getting back to me

-- The drug is chlorcyclizine (link to license ann't below), and the public interest group, Knowledge Ecology International (which often looks at NIH licenses) is complaining that its request for "reasonable pricing" requirements in the license were brushed aside to the detriment of taxpayers. The group has just received a public records request (a portion is attached) and suggests they show that NIH is worried more about scaring off the licensee than benefiting the taxpayers who funded this drug and have no assurance they won't have to pay excessively high prices for it.

-- I'm looking for an agency response to this contention.

-- My deadline is 10/28/16 at 5 PM EDT

-- My questions would basically be:

How do you respond to their complaint?

What are the institute's priorities when licensing these drugs?

How much progress has this licensee made on marketing this drug?

What were the results of the Phase 1 trial that NIH funded on this drug?

Some observers are asking: why grant an exclusive license to a small, unknown company with no track record of bringing drugs to market?

I'd have follow-ups depending on the answers, natch, and would want to hear any responses to smarter questions on all this that your folks might have.

Any help appreciated,

Dan Vergano
BuzzFeed News
b6

Dan Vergano | Science Reporter (DC) [b6]
BuzzFeed
1630 Connecticut Ave. 7th Floor, Washington DC 20009

link: <https://s3.amazonaws.com/public-inspection.federalregister.gov/2015-06974.pdf>

Dan Vergano | Science Reporter (DC) [b6]
BuzzFeed
1630 Connecticut Ave. 7th Floor, Washington DC 20009

On Mon, Oct 24, 2016 at 11:57 AM, Payne, January (NIH/NIDDK) [E] <january.payne@nih.gov> wrote:

Dear Dan,

Thanks for your message. Can you please provide more information so I can look into your request?

- What is the drug name, and can you please briefly describe the issue that has been raised? Also, what is the name of the public interest group?
- What is your hard deadline?
- Can you please provide a few examples of questions you'd like to ask?

Best,

January W. Payne

Office of Communications and Public Liaison
National Institute of Diabetes and Digestive and Kidney Diseases

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<image001.jpg>

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From: Dan Vergano [mailto:dan.vergano@buzzfeed.com]
Sent: Monday, October 24, 2016 11:25 AM
To: NIDDK NIDDKMEDIA (NIH/NIDDK) <niddkmedia@niddk.nih.gov>
Subject: Fwd: BuzzFeed News: press contact / licensing

Krysten's email responder suggested I send this note to this contact. I have also left a phone message with the press office. I am looking for comment this week.

Ms. Carrera,

I'm a science reporter at BuzzFeed News. I'm looking for a press contact at NIDDK who can address a drug licensing issue at your institute. A public interest group is raising questions about one of your licenses and I'd like to get a response from the institute.

Thanks for any help,

Dan Vergano

BuzzFeed News

b6

Dan Vergano | Science Reporter (DC) | b6
BuzzFeed
1630 Connecticut Ave. 7th Floor, Washington DC 20009

JANUARY PAYNE

Senders C...

@ National Institutes of Health

[National Institutes of Health | 9000 Rockville Pike, Bethesda, MD 20892, USA](#) | Official website of the National Institutes of (NIH). NIH is one of the world's foremost medical research centers. An agency of...



January Payne on LinkedIn



[@NIH | 663K followers | 6K tweets](#) - 3 hours ago

There's still time to submit your @NIH_LRP application! Get started on yours today. Deadline is Nov.15 bit.ly/2e7QDzt #studentdebt



[Search for January Payne on Google](#)

Dan is using Senders. [View / edit your own Card](#)

<Reasonable Pricing - Virotas NIH .pdf>

From: Joe Allen [jallen@allen-assoc.com]
Sent: 1/21/2016 4:42:39 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=OD/cn=ROHRBAUM]
Subject: Milbank Quarterly article on march in's that cites us
Attachments: March-in rights in Milbank Quarterly quoting me.pdf

I got the attached the other day from some university associations and just scanned to the end to see what it says. I was startled when going through some old emails on another project to see that they had interviewed me! They also say they talked with you. While they maintain that it's ambiguous whether or not we intended to use march in's for drug price controls , at least they conclude that Bayh-Dole is not the appropriate tool for that purpose.

Let's get together at AUTM. I'm just starting to put together my schedule. Any days and times that are good for you?

Thanks

--

Joseph P. Allen
President
Allen and Associates
60704 Rt. 26, South
Bethesda, OH 43719
(w) 740-484-1814
(c) [REDACTED] b5
www.allen-assoc.com

Original Investigation

Do March-In Rights Ensure Access to Medical Products Arising From Federally Funded Research? A Qualitative Study

CAROLYN L. TREASURE, JERRY AVORN,
and AARON S. KESSELHEIM

Brigham and Women's Hospital and Harvard Medical School

Policy Points:

- The Bayh-Dole Act of 1980 formalized the ability of institutions receiving federal research funding to commercialize discoveries by issuing exclusive licenses for patents that emerge. This legislation also contained a march-in rights provision, allowing the US government to cancel the exclusive license if the product was not available to the American public on reasonable terms.
- Since 1980, there have been 5 march-in rights petitions for 4 different health care-related products, most recently in cases of drugs discovered with federal funding made available only at exorbitant prices. The National Institutes of Health (NIH) has rejected each petition. In our qualitative analysis of experts and participants involved in these march-in rights petitions, we found little prospect NIH will ever invoke march-in rights in such cases.

Context: The high cost of new prescription drugs and other medical products is a growing health policy issue. Many of the most transformative drugs and vaccines had their origins in public-sector funding to nonprofit research institutions. Although the Bayh-Dole Act of 1980 provides for “march-in rights” through which the government can invoke some degree of control over the patents protecting products developed from public funding to ensure public access to these medications, the applicability of this provision to current policy options is not clear.

Methods: We conducted a primary-source document review of the Bayh-Dole Act’s legislative history as well as of hearings of past march-in rights petitions

The Milbank Quarterly, Vol. 93, No. 4, 2015 (pp. 761–787)

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to the National Institutes of Health (NIH). We then conducted semistructured interviews of 12 key experts in the march-in rights of the Bayh-Dole Act to identify the sources of the disputes and the main themes in the statute's implementation. We analyzed the interview transcripts using standard qualitative techniques.

Findings: Since 1980, the NIH has fully reviewed only 5 petitions to invoke governmental march-in rights for 4 health-related technologies or medical products developed from federally funded research. Three of these requests related to reducing the high prices of brand-name drugs, one related to relieving a drug shortage, and one related to a potentially patent-infringing medical device. In each of these cases, the NIH rejected the requests. Interviewees were split on the implications of these experiences, finding the NIH's reluctance to implement its march-in rights to be evidence of either a system working as intended or of a flawed system needing reform.

Conclusions: The Bayh-Dole Act's march-in rights continue to be invoked by policymakers and health advocates, most recently in the context of new, high-cost products originally discovered with federally funded research. We found that the existence of march-in rights may select for government research licensees more likely to commercialize the results and that they can be used to extract minor concessions from licensees. But as currently specified in the statute, such march-in rights are unlikely to serve as a counterweight to lower the prices of medical products arising from federally funded research.

Keywords: march-in rights, Bayh-Dole Act, government-funded research, National Institutes of Health.

RESEARCH FUNDED BY US TAXPAYERS HAS CONTRIBUTED TO the development of some of the most transformative drugs available to patients, including the anticancer drug imatinib (Gleevec), tumor necrosis factor blockers such as infliximab (Remicade) and etanercept (Humira) useful in inflammatory rheumatological and gastroenterological diseases, and vascular endothelial growth factor inhibitors like bevacizumab (Avastin) for cancer and eye diseases.¹ One comprehensive review of patent records found that government resources had directly contributed to the discovery of 153 marketed drugs and vaccines, including some of the most transformative medicines developed in the past 20 years.² Commercialization of products based on such government investment was the central purpose of the Bayh-Dole Act of 1980, which allowed universities to patent the results of federally

funded research and then to license these patents to commercial entities, encouraging the institutions to claim those rights to promote the commercialization of the inventions.

The Bayh-Dole Act also included a controversial provision intended to ensure that the final products emerging from this government-sponsored research would be available to the public on reasonable terms. This provision was known as *march-in rights*, which enable the government to intercede in exclusive license contracts generated in relation to products that are based on public financial support. Before the Bayh-Dole Act, patents obtained on federally funded work remained in the government's control, although concern grew that the government was not actively seeking licenses to develop commercial products and there was not a consistent licensing protocol across government agencies. In the 1960s and 1970s, the National Institutes of Health (NIH) and a small number of research universities designed institutional patent agreements to transfer the patent title to the universities to encourage more active development. In these agreements, the government in theory maintained march-in rights to reclaim the invention if the licensees were not taking adequate steps to commercialize the product or meeting the needs of American consumers. This would enable the government to take control of the invention, and cancels the grant of an exclusive license for a product that its funds helped develop. In doing so, the government regains the authority to relicense the intellectual property to another party. This process of contingent patent title transfer with march-in rights was formalized when the Bayh-Dole Act made the process consistent across all federal agencies.

In recent years, the possibility of exercising Bayh-Dole's march-in rights has been invoked most consistently in the context of high-cost medical products based on public funding of research at nonprofit institutions. Clinicians and policymakers continue to express concern about the prices of new drugs for cancer,³ essential genetic tests,⁴ and medical devices.⁵ In July 2013, Senator Patrick Leahy (D-Vt.) submitted another petition relating to Myriad's ownership of a genetic test for the BRCA gene, which predicts predisposition to breast and ovarian cancer, after Myriad sought to block competition in the wake of the US Supreme Court's invalidation of its genetic code patents.⁶ Senator Leahy argued that the essential discoveries leading to Myriad's test were developed with government funding, yet the test was too expensive for millions of women. He believed this insufficient access could be remedied using the

government's march-in rights. In 2014, an economist and law professor made a similar argument related to the cost of sofosbuvir (Sovaldi),⁷ the \$1,000-per-pill treatment for hepatitis C virus sold by Gilead Pharmaceuticals. It had originally been discovered by a company founded by a faculty member at Emory University, much of whose work on the usefulness of nucleoside viral inhibitors was federally funded.⁸ In these and other cases, some have argued that US patients are in effect paying twice, once for the research and a second time for the high prices of the products, which were made possible by that research.^{9,10}

While march-in rights were codified in the 1980 legislation, the complex political process leading up to the passage of the Bayh-Dole Act¹¹ left the scope of their applicability unclear, including whether they could be used to reduce high consumer prices on products originating from government-sponsored research. In the more than 3 decades since the Bayh-Dole Act, petitions for the government to consider march-in rights have been publicly considered only 5 times for 4 different products—and rejected by the NIH each time. Given this lack of clarity about march-in rights, we sought to examine their role in the licensing and commercialization of health care-related government discoveries and whether using march-in rights is a viable strategy to address the rising costs of certain health care products. In an earlier report, we provided an overview of petitions to invoke the clause relating to health care products.¹² For this qualitative analysis, we conducted semistructured interviews with key participants in the development of the Bayh-Dole Act and the march-in rights appeals. Our goal was to understand the dynamics of seeking march-in rights and their role in the commercialization of innovative medical technology based on government-funded research.

Methods

Data Sources

We first sought all publicly available documents related to the development of the Bayh-Dole legislation by reviewing US government databases holding primary source documents concerning the act, in addition to PubMed and the legal literature (LexisNexis).

Next we reviewed records of past hearings for march-in rights petitions that were publicly considered by the government that were related

to health care technology. We did not investigate potential applications of the march-in rights in other contexts such as defense, environmental policy, and aerospace.

Qualitative Data Collection

We then conducted semistructured interviews with experts, including key participants in the development of the legislation and the disposition of past petitions,¹³ inquiring about Congress's intent in creating the march-in rights provision, the rationale for past march-in rights petitions, the NIH's role in evaluating march-in rights petitions, the criteria on which march-in rights petitions are evaluated, and recommendations to improve the usefulness of the march-in rights policy and the Bayh-Dole Act itself.

We identified 21 potentially relevant experts in the Bayh-Dole Act and march-in rights from the fields of politics, law, business, and health care and public health. Twelve agreed to participate, with at least 2 participants representing each of the 4 main categories of expertise (Table 1). The median time for the telephone interviews was 46 minutes, with a range of between 21 and 64 minutes. Two of the investigators (CLT and ASK) took notes during the interviews, recorded the interviews, and later transcribed them. The study was approved by the ethics review board at Brigham and Women's Hospital.

Data Analysis

We began by collecting the details of the march-in rights cases and identified common keywords and themes regarding the march-in rights process. Then, using these keywords, we analyzed the interview transcripts using standard qualitative coding techniques.^{14,15} Based on a subset of 3 randomly selected interviews, we independently developed coding schemes for organizing the data.¹⁶ These were then compared and reconciled (NVIVO software package, QSR International, Melbourne, Australia) to produce a final coding structure that encompassed (1) Congress's intent of the march-in rights provisions, (2) the decision and steps to file a march-in rights petition, (3) the applicability of march-in rights to the pricing and patient access issues, (4) the decision to reject a petition, and (5) recommendations for improving the applicability of march-in rights as a public policy tool.

Table 1. List of Experts in Bayh-Dole Act and March-In Rights Petitions

Name	How Identified (expertise)	Current Position	Summary of Role
Joseph Allen	Bayh-Dole literature (politics)	President of consulting firm focused on US technology transfer	Helped draft Bayh-Dole Act as member of Senator Birch Bayh's staff
Allen Black, JD	NIH record search (law)	Private patent attorney	Key author of agalsidase beta petition
Howard Bremer, JD	NIH record search (politics, law)	Wisconsin Alumni Research Foundation (WARF), emeritus patent counsel	Helped draft Bayh-Dole Act
Curt Civin, MD	NIH record search and medical literature (health care / public health)	Professor at University of Maryland School of Medicine	Discovered the antibody technology licensed to Baxter that was the basis for the CellPro petition
Robert Cook-Deegan, MD	Medical literature (health care / public health)	Research professor, Duke University	Academic research on patents and technology transfer
James Love	Medical literature, NIH record search (health care / public health)	President of Knowledge Ecology International	Key author of ritonavir and latanoprost petitions

Continued

Table 1. *Continued*

Name	How Identified (expertise)	Current Position	Summary of Role
Barbara McGarey, JD	Medical literature (law)	General counsel for public health, National Institutes of Health (NIH)	Deputy director, NIH Office of Technology Transfer during the CellPro petition
Richard Murdock	Medical literature (business)	American business executive	President of CellPro at time of petition
John Raubitschek, JD	Referral (politics, law)	Attorney for Defense Procurement and Acquisition Policy Division, US Department of Defense	Helped draft regulations to implement Bayh-Dole Act
Daniel Ravicher, JD	NIH record search (law)	Executive director, Public Patent Foundation	Provided testimony related to first ritonavir petition
Mark Rohrbaugh, PhD, JD	NIH record search (law)	Director, NIH Office of Technology Transfer	Oversees office that has responsibility for reviewing march-in rights petitions

Continued

Table 1. *Continued*

Name	How Identified (expertise)	Current Position	Summary of Role
Teri Willey, MBA	Referral, NIH record search (business)	Vice president, Mount Sinai Innovation Partners	Past president, Association for University Technology Managers, helps manage agalsidase beta license at Mount Sinai School of Medicine's technology transfer office

Names are in alphabetical order. The presence of an interview source on this list does not imply endorsement of the article or its findings.

Results

The Bayh-Dole Act and March-In Rights

The Bayh-Dole Act instituted a government-wide policy allowing academic recipients of federal funding to seek patents on inventions developed with that funding. Universities or academic medical centers were then obligated to license the patents exclusively to small business owners and nonprofit research institutions for the purpose of development.^{17,18} In 1983, the law was expanded by executive order to include large corporations.

Lawmakers also gave the government the right to "march in" and exercise its residual intellectual property rights in the invention. By marching in, the government would grant an open license on the intellectual property with the expectation that another commercial entity would be able to develop and market the product. The law spelled out

4 circumstances in which this power could be used: to reclaim an invention when the licensee had not taken, or was not expected to take within a reasonable time, effective steps to achieve practical application (Clause 1), to “alleviate health or safety needs” not being reasonably satisfied by the licensee (Clause 2), to comply with federal laws or regulations requiring some public use of the invention (Clause 3), and to remedy a licensee’s failure to meet the domestic manufacturing requirement (Clause 4).¹⁹ In Clause 1, the term *practical application* is defined in 35 USC §201(f) as “establish[ing] that the invention is being utilized and that its benefits are . . . available to the public on reasonable terms.”

Any party that believes a patent license holder has not met 1 of the 4 criteria can submit a march-in request to the appropriate US government agency, which, in the case of health care products, is usually the NIH. After receiving a petition, the agency considers whether to initiate the march-in proceedings. The process begins with an official notice sent to the licensee, which then has 30 days to respond. If the response includes a dispute over the charges, a fact-finding process is conducted that “shall be as informal as practicable and be consistent with principles of fundamental fairness,” including such principles as the right of counsel.²⁰ The contractor has the right to appeal to the federal courts a decision to exercise march-in rights. By contrast, petitioners do not have the right to appeal the decision to not exercise march-in rights.¹⁹

Outcomes of Past March-In Rights Petitions

CellPro Petition for Ceprate SC (1997). The first time that march-in rights were seriously considered for a health care technology arose from a dispute between a start-up biotechnology company, CellPro, and Baxter Healthcare Corporation, a large medical products manufacturer. The technology at issue was discovered by a pediatric oncologist, Curt Civin, and his colleagues at the Johns Hopkins School of Medicine. Conducting research in 1981 funded by the National Cancer Institute, other foundation grants, and institutional support, Civin and his team developed a series of monoclonal antibodies against an antigen family (CD34) on undifferentiated stem cells. One of those antibodies was IgG myeloid-10 (My-10). The antibody was potentially useful in treating hematologic malignancies like leukemia because it could help separate undifferentiated stem cells from cancerous descendant cells during a

bone marrow transplant. Johns Hopkins filed a patent application in 1984, which was granted for the My-10 antibody and other antibodies that recognize the CD34 antigen. According to Civin, “We patented the antibody itself and the whole class of antibodies against CD34. We patented the antigen. We patented the cells and we patented the procedure for the technology for immunopurifying hematopoietic stem cells from the bone marrow.”²¹ Johns Hopkins licensed these patents to Becton-Dickinson & Company.

The march-in rights controversy arose because after Civin’s discovery of My-10, scientists at the Fred Hutchinson Cancer Research Center in Seattle created an IgM monoclonal antibody against CD34, called 12-8, that recognized a CD34 binding site distinct from My-10’s binding site. The 12-8 antibody was described in the literature in 1986 but not patented.²² It was useful in a process developed and patented by Hutchinson scientist Ronald Berenson to purify CD34-positive stem cells using the proteins biotin and avidin. Berenson’s technology formed the basis for creating CellPro, which developed the technology into the Ceprate SC tool for separating bone marrow cells.

CellPro knew early on that the Hopkins patents existed, although it received legal counsel that those patents were invalid because they were too broad, covering antibodies to CD34 that Civin did not discover, and because they were publicly disclosed more than a year before the application. Nonetheless, CellPro sought licenses for the patents, first from Becton-Dickinson and then in January 1992 from Baxter, to which Becton-Dickinson had exclusively sublicensed the patents. Baxter offered a nonexclusive license to CellPro for a greater royalty than it received from other licensees, perhaps because Baxter saw CellPro as a potential competitor. The companies could not reach agreement, and CellPro preemptively sued to invalidate the Civin patents in April 1992.²³ CellPro’s Ceprate SC was approved by the US Food and Drug Administration (FDA) in 1996.

In March 1997, as the years of patent litigation were reaching their conclusion, CellPro requested that the NIH assert its march-in rights and grant an open license to the Civin My-10 patents. CellPro cited Clause 1 (to reclaim an invention that had not been developed or commercialized in a reasonable length of time) and Clause 2 (to alleviate health or safety needs not being reasonably satisfied by the licensee) as the bases for its petition. CellPro pointed to the long delays in Baxter’s development, the licensing terms that Baxter offered to it, and the fact that it had an

approved and marketed technology. By contrast, Baxter's Isolex had only recently filed for FDA approval, in February 1997. CellPro supported its claims by pointing to Johns Hopkins's controversial patents, claiming, "CellPro does not use the My-10 antibody discovered by Dr. Civin. It is only because the patent claims were written too broadly . . . that there is even an issue." After the petition was filed, former Senator Birch Bayh (D-Ind.), cosponsor of the Bayh-Dole Act, wrote a letter to the NIH supporting CellPro's request for march-in rights use "to ensure that an important new medical product will be available for use in this country."²⁴

The NIH investigated the matter in detail to determine whether Baxter had failed to take, or was not expected to take within a reasonable time, effective steps to achieve practical application of the subject invention (Clause 1) and whether a public health or safety need was not reasonably satisfied (Clause 2). The NIH concluded that Baxter had a promising product in development and ultimately secured a promise from the company to allow Ceprate on the market until Isolex was approved by the FDA (which occurred in 1999). Thus, in August 1997, the NIH did not initiate the formal proceedings to invoke march-in rights. The NIH remarked that it was wary "of forced attempts to influence the marketplace for the benefit of a single company, particularly when such actions may have far-reaching repercussions on many companies' and investors' future willingness to invest in federally-funded medical technologies."²⁵

The NIH's decision was a final blow to CellPro, which had received in the previous month a federal district court decision upholding Hopkins's patents and finding CellPro guilty of willful patent infringement.²⁶ CellPro paid a penalty of more than \$15 million, was forced to file for bankruptcy, and went out of business. No entity purchased the rights to the Ceprate system out of bankruptcy, and Baxter later withdrew Isolex from the market.

Essential Inventions Petitions for Ritonavir and Latanoprost (2004). Both the second and third petitions in our review were submitted in 2004 by Essential Inventions, a nonprofit organization. The first petition concerned ritonavir, an HIV protease inhibitor, which was developed partially through a \$3.5 million grant from the National Institute of Allergy and Infectious Diseases (NIAID) to Abbott Laboratories from 1988 to 1993. The objective of the grant was to investigate whether medicines could be created to block HIV protease enzymes and inhibit

the spread of AIDS. Abbott received this grant under the National Cooperative Drug Discovery Group for AIDS, a federally chartered program created in response to the HIV/AIDS health crisis in the 1980s. The purpose of this funding was to promote synergy among government, industry, and academic laboratories to translate basic research findings regarding HIV into novel antiretroviral therapies. According to Abbott's principal investigator, this grant "catalyzed the development of the antiretroviral program."²⁷

The Abbott scientists' work was successful, and the FDA approved ritonavir in 1996. It was originally prescribed as a component of highly active antiretroviral therapy (HAART), even though the drug's adverse effects—gastrointestinal symptoms, paresthesias, and elevated serum triglycerides—greatly limited its use.²⁸ The viability of ritonavir in the marketplace, however, was saved by another characteristic of the drug: its ability to work as a pharmacokinetic enhancer of other protease inhibitors. Even at a very low dose, ritonavir inhibited the cytochrome P450-3A4 enzymatic system in the liver. Physicians began using, and Abbott began promoting, low-dose ritonavir dosing schedules that potentiated the activity of other protease inhibitors used in HAART—most of which were metabolized in the same enzymatic system—while avoiding ritonavir's side effects. In 2000, Abbott received approval for a new protease inhibitor, lopinavir, in a fixed-dose combination pill with low-dose ritonavir, which it called Kaletra. Abbott did not market stand-alone lopinavir.²⁹

The controversial move leading to the march-in case occurred in 2004. In prior years, Abbott had set a price for ritonavir of \$2.14 per unit, in line with the other protease inhibitors. But in 2004, Abbott abruptly increased ritonavir's price for US consumers to \$10.71 per unit, raising the annual cost of the drug from about \$9,000 to \$50,000. Yet, Abbott did not similarly adjust the price of Kaletra, even though it included ritonavir. As a result, Kaletra became the least expensive protease inhibitor regimen for US patients that included the ritonavir-boosting supplement.

The march-in request for Abbott invoked Clauses 1 and 2 in the Bayh-Dole Act and claimed "that the patent owner charges unreasonable prices for ritonavir, harming the public."²⁹ Essential Inventions argued that by raising the price to such a degree, which created barriers to access the drug, Abbott harmed HIV patients taking ritonavir in conjunction with other protease inhibitors as part of HAART. In

particular, the higher drug prices reduced patients' adherence, essential in HIV regimens to prevent resistance. The organization also argued that Abbott acted anticompetitively by compelling patients to switch to the fixed-dose Kaletra even if another protease inhibitor was a better fit. Last, Essential Inventions saw this petition as a way to start addressing a broader pricing issue, that products resulting from "government-funded investments are routinely being priced higher in the United States than they are in foreign countries."²⁹

After hearing preliminary testimony from relevant parties—including Senator Bayh, who this time argued against the exercise of march-in rights—the NIH concluded that Abbott met the standard for achieving practical application of ritonavir based on the drug's availability for sale and its widespread use by HIV/AIDS patients. The NIH concluded "that the extraordinary remedy of march-in is not an appropriate means of controlling prices . . . [that should be] left for Congress to address legislatively." It rejected the petition. The NIH considered that the alleged anticompetitive behavior would be better reviewed by the Federal Trade Commission (FTC). Private antitrust lawsuits later filed against Abbott's pricing schemes were dismissed in 2009. In the wake of this petition, Abbott agreed to exempt government purchasers, both federal Medicaid and state-run AIDS drug assistance programs, from the price increase. Pharmaceutical insurers and patients without prescription drug insurance thus became the main payers of the increased price.³⁰ Abbott also expanded, through its charity program, the eligibility criteria for people seeking ritonavir.

In 2012, a second, follow-up, petition was filed for ritonavir. In it, civil society organizations argued that US consumers were being charged 400% more than other high-income countries for the drug, creating barriers to patient access and placing US employers at an economic disadvantage with overseas competitors.³¹ In 2013, this petition was rejected by the NIH. The NIH concluded that AbbVie (Abbott's new name) had achieved "practical application of Subject Patents," since the drug was available for use and AbbVie had started a "Patient Assistance Program" to help patients who could not afford Norvir.³²

Shortly after Essential Inventions filed its first ritonavir petition in 2004, it filed another, similarly framed petition concerning Pfizer's glaucoma medicine, latanoprost (Xalatan). Latanoprost was developed with more than \$4 million in NIH research grant funding to Laszlo Bito, then an associate professor of ocular physiology at Columbia University.

During the late 1970s and early 1980s, Bito's laboratory developed a compound that reduced abnormally elevated intraocular pressure. After successful testing in animal models, Bito realized the therapeutic potential of this compound as a treatment for glaucoma, and Columbia filed for a patent on the compound in 1982. Columbia's patent contains specific language identifying the invention as developed under research supported by the National Eye Institute. Latanoprost was subsequently exclusively licensed from Columbia University to Pharmacia Corporation in 1983. Pharmacia was acquired by Pfizer in 2003.³³

The march-in petition against latanoprost claimed that the US prices of the drug were 2 to 5 times higher than in other high-income countries—invoking Clauses 1 and 2—despite US taxpayers' funding its early development. In 2004, a 2.5 mL bottle cost \$19.56 in Canada but \$50.99 in the United States. The petition argued that the “reasonable terms” clause implied a reasonable price and that this discriminatory pricing was causing disparities in access, creating a public health crisis.

The NIH disagreed. It rejected the petition for march-in rights use, claiming that Pfizer met the standard for achieving practical application and reiterating its contention from the Abbott case that the march-in process should not be a means of controlling prices.

Fabry's Disease Patients' Petition for Fabrazyme (2010). In the fourth petition, patients with Fabry's disease requested an open license for agalsidase beta (Fabrazyme), the only enzyme replacement therapy approved by the FDA to treat this disease. Fabry's disease is a hereditary lysosomal storage disease characterized by a lack of alpha-galactosidase enzyme. Chronic enzyme replacement therapy can allow patients to avoid end-stage renal disease, cerebrovascular damage, severe neuropathic pain, and cardiovascular manifestations such as left ventricular hypertrophy, heart failure, and valve abnormalities.³⁴ Agalsidase beta enzyme replacement therapy was developed by Robert Desnick and others at the Mount Sinai School of Medicine with more than \$4.1 million in NIH funding. Desnick patented the compound in 1990 and then licensed it exclusively to Genzyme, which further developed and commercialized it.

The FDA approved agalsidase beta in 2003. Another enzyme replacement therapy for Fabry's disease, agalsidase alfa (Replagal), was approved in Europe in 2001. Made by Shire, it was never submitted to the FDA for approval after the FDA granted orphan-drug status to Fabrazyme, which gave Genzyme 7 years of market exclusivity from competitors seeking to market the same drug for the same condition.³⁵ After losing

the race to market in the United States, Shire withdrew its product from consideration in the United States and focused on Europe.

The controversy leading to the march-in rights petition emerged from a crisis in 2009, when viral contamination in a Genzyme manufacturing facility in Massachusetts shut down production. As a result, Genzyme could produce only enough of the drug to meet 38% of the US demand, and patients had to ration their treatment. Accordingly, dosage was cut by 62%, and no new patients were allowed to start taking agalsidase beta.

In 2010, 3 patients with Fabry's disease petitioned the NIH to exercise its march-in rights, invoking Clauses 1 and 2. The petitioners argued that Genzyme "has not satisfied and cannot reasonably satisfy the health and safety needs of Fabry patients by rationing drugs while preventing additional sources of manufacture." Indeed, they found evidence that during the shortage, Genzyme sent the majority of its agalsidase beta produced in US facilities to meet its obligations in Europe so that it could continue to compete with Shire's agalsidase alfa. The petitioners believed that these actions demonstrated that Genzyme was not taking steps to achieve practical application of the invention.

The NIH rejected the petition on December 2, 2010, and did not consider march-in rights use, claiming that granting the petition would not "address the problem identified by the Requestors." The NIH argued that granting an open license through march-in rights would not increase the supply of Fabrazyme in the short term. At this time, Shire offered to manufacture and market agalsidase alfa (Replagal) in the United States, since this drug's efficacy was similar to Genzyme's agalsidase beta in treating Fabry's disease in Europe. But the FDA would not approve it based on the European data alone and requested a clinical trial comparing agalsidase alfa and agalsidase beta. Neither company wanted to pursue this because of the financial cost and market-share ramifications. As the shortage continued, the petitioners filed a citizen petition, asking the FDA to approve agalsidase alfa for short-term use. In its response to the march-in rights petition, the NIH did not directly address the potential for agalsidase alfa use in the United States. It maintained that if a company had a viable plan to obtain FDA approval for agalsidase beta during the period that Genzyme was not able to meet demand, the NIH would reconsider its decision not to exercise its march-in authority. The NIH also cited Genzyme's claim that full production would return in early 2011 and stated that it would monitor

Genzyme's production efforts by receiving monthly reports from the original licensor, Mount Sinai. Ultimately, the shortage was resolved in 2012 after Genzyme addressed the contamination. In July 2014, Knowledge Ecology International submitted a letter to the FTC urging it to investigate the "decision made by Shire not to compete in the US market for Fabry's disease treatments."³⁶

Two Views of March-In Rights

Our interview responses generally fell into two main categories with respect to the questions of how march-in rights have functioned in the past and their role in the marketplace. One group of interviewees saw march-in rights as an extreme option intended to address only situations in which products were truly unavailable and as inapplicable to situations characterized by high prices alone. The other major perspective favored applying march-in rights to help address major inequities in the cost and availability of health care products arising from federally funded research. Table 2 presents representative quotations from each point of view.

March-In Rights Work Well, Are Not Intended for Price-Setting. One of the two dominant themes was that the current commercialization system under Bayh-Dole is achieving its intended purpose, as evidenced by the many products that have arisen from federally funded research since 1980. To these interviewees, the policy was intended to ensure commercialization, so that developments "were not left on the shelf," with the march-in rights serving as a safeguard to protect against a very narrow set of highly undesirable outcomes, such as products being acquired and intentionally not developed. To these interviewees, the fact that march-in rights have never been used does not mean that the policy is not working; instead, it is evidence of a system working as intended, in that the march-in rights cast a powerful shadow over users of government-sponsored research, making it less likely that companies obtaining the rights to this research would conduct themselves in ways that undermined the public's health. In particular, these interviewees argued that march-in rights have empowered grantees, commonly academic centers, to engage in the oversight of licensed products, which has likely led to the selection of better developers.

Those interviewees adhering to this view of march-in rights also pointed out that the NIH's consideration of march-in rights petitions

Table 2. Representative Quotations Supporting and Opposing Use of March-In Rights to Address High Prices of Health Care Products Arising From Federally Funded Research

Topic	Interviewees' Responses	Interviewees' Responses
	Believing March-In Rights Not Intended for Price-Setting	Believing March-In Rights Applicable to Addressing High Prices
Are high prices of government-sponsored discoveries a problem?	"If you look at all the public policy issues surrounding drug pricing and access to healthcare it's a much bigger issue. [This pricing issue] doesn't really get solved by having a subset of inventions and healthcare products and diagnostics or treatments or vaccines that arise out of NIH-funded research."	"We found that 13 of the 14 drugs that we looked at with government rights in them were priced higher in the United States than in any other country. . . . Pricing is a broad issue. Government funded investments are routinely being priced higher in the United States than they are in foreign countries . . . countries we compete against in the market."
Role of government in drug pricing	"Our concern under Bayh-Dole was 'We want to make sure these things are being used. We want to get them off the shelf. Get them out there where the taxpayers can use them.' That was really the essence of Bayh-Dole. We had no interest at all in trying to regulate what the prices could be because that's a whole different thing—I don't even know how you would do that, but you certainly wouldn't do it under a tech transfer bill."	"The federal government should consider rising health care costs when considering march-in . . . Bayh-Dole just opened the floodgates for federal funding to private companies. But there's got to be some measure of control over that. There are cases where it [march-in process] absolutely should be granted . . . for the purpose of making sure that the government-funded technology is efficiently and appropriately developed."

Continued

Table 2. *Continued*

Topic	Interviewees' Responses Believing March-In Rights Not Intended for Price-Setting	Interviewees' Responses Believing March-In Rights Applicable to Addressing High Prices
Bayh-Dole statutory language	“Reasonable terms’ means reasonable terms in the license . . . pricing should not be considered.”	“What is ‘reasonable terms’? Can you imagine what kind of reasonable terms are you talking about? Charging Americans 400 times more than foreigners? The law says ‘Available to the public on reasonable terms.’ What does ‘available to the public’ mean? It means something, right?”
Feasibility of march-in rights being invoked	“I think [march-in rights] play an important background role . . . primarily as a warning or potential punishment to those who would violate the statute.”	“The value of the march-in seems to be almost exclusively as a negotiating tool, but nobody really thinks that it has any credibility as such a tool because nobody ever expects NIH to march-in.”
		“I also think NIH has absolutely zero competence and zero interest in getting involved in access to healthcare products and services. They’re a research agency and the whole norm of the culture at NIH is supportive research and much less about making sure that it gets incorporated equitably into the healthcare system.”

in the Abbott and CellPro cases led to minor concessions on the part of the rights holders, as Abbott agreed to lower the price of ritonavir for certain US government purchasers and Baxter agreed to let the CellPro device remain on the market until its own product was approved by the FDA. Thus, these respondents felt that the existence of march-in rights, even without their fulfillment, would motivate parties to uphold the public health goals of the Bayh-Dole Act.

These interviewees ascribed the government's hesitancy to intervene through march-in rights as being related to the negative ramifications of the product development process. They discussed the uncertainty and expense inherent in the innovation process and theorized that granting march-in rights more readily would deter future participants from commercializing other government-sponsored research. They offered the justification that an exclusive license that could be broken in extreme circumstances could shake a licensee's confidence in acquiring the license and subsequently investing the substantial sums required to develop the product and to conduct the clinical trials needed to bring a therapeutic to market. In addition, the development of a marketable product from licensed patents inevitably generates a considerable amount of know-how leading to more patents that would not be covered by march-in rights, as illustrated in the Fabrazyme march-in case. To some interviewees, these facts support the impracticality of applying march-in rights to marketed products.

The interviewees pointed to the NIH's public responses to these 5 march-in cases as confirmation that it has been consistent in asserting its unwillingness to become a "price-setting" agency. Indeed, they argued that granting march-in rights is outside the scope of the NIH as a research-funding agency and that it does not have the institutional competence to police development contracts of its extramural grantees. As additional evidence of the potential problems that might arise were the NIH to move beyond its traditional role and regulate drug prices, 2 interviewees cited an episode from 1989 when the NIH adopted a "reasonable pricing clause" in its cooperative research and development agreements (CRADAs) in response to the outcry over the high price of zidovudine (AZT or Retrovir). Zidovudine was discovered by Jerome Horwitz at the Karmanos Cancer Institute in Michigan, and it was then shown to be active against HIV based on testing led by Samuel Broder at the NIH. But zidovudine was sold for \$8,000 per year by Burroughs Wellcome as the HIV epidemic spread, beyond what many patients

with HIV could afford, particularly with an estimated 35% having no prescription drug insurance at the time.³⁷ The CRADA pricing policy was then eliminated in 1995 based on widespread recognition that it was causing the industry to avoid even potentially beneficial collaboration with government scientists.

In summary, the interviewees endorsing this narrative believed that march-in rights were intended to be a tool to promote commercialization. Thus, they argued, as long as technologies on the market are being sold, even if the price is somewhat higher than consumers would like, the goal of the Bayh-Dole Act has been achieved. These interviewees interpreted the text of the march-in rights provision as not suggesting that high prices justified the use of march-in rights. They often cited later comments on this issue by Senators Birch Bayh and Robert Dole (R-Kans.): "Bayh-Dole did not intend that government set prices on resulting products. The law makes no reference to a reasonable price that should be dictated by the government."³⁸

"Reasonable Terms" Should Include Price. The other primary perspective offered by a different set of interviewees was that the march-in rights provision could reasonably be applied to address serious inequities in the prices of products originating from federally funded research. According to this view, the Bayh-Dole Act led to an increase in commercialization, and march-in rights were established to ensure that US citizens could access the benefits of federally funded developments. Since tax dollars contribute to health care innovation both indirectly and directly,³⁹ they argued, the US public has the right to access these technologies under reasonable terms, which can imply reasonable prices in certain circumstances. Yet, access on reasonable terms has not always been met.

Two interviewees traced the origin of ambiguity in the "reasonable terms" language to the development of the law. The Bayh-Dole Act originally pertained to small business owners and nonprofit research institutions. It was later expanded to include large for-profit companies via an executive order from then President Ronald Reagan. This might explain why the potential for profit incentives to lead to higher drug prices was not explicitly addressed in the writing of the law, even if the discussion before the law's passage suggested that legislators considered it to be incorporated in the act's language.

These interviewees pointed to the outcomes of these 5 petitions as evidence that the system was structured so as to discourage implementing march-in rights. For example, in the march-in procedure, the patent

holder can appeal the granting of the request to the courts, whereas the petitioner does not have the appeal option if the petition is rejected. This asymmetry could be a deterrent to march-in rights petitions as well as to the NIH's invoking march-in rights. Furthermore, this group of interviewees also noted that the NIH is not equipped to address and implement a request for march-in rights. The NIH does not have the capability or the human capital to perform the detailed economic analysis and regulatory navigation required to implement a march-in request. Thus, the interviewees believed that there had been clear instances in which march-in petitions should have been filed and march-in rights should have been used but that procedures favoring inaction had deterred their use.

Finally, these interviewees suggested that in certain instances, the march-in rights policy should be used to control the high prices of health care products developed from federal funding, since unaffordable health care products can create disparities in access that warrant the use of march-in rights. This view is based on the language requiring a contractor to provide the inventions "upon terms that are reasonable under the circumstance." These interviewees noted that the intention of the statutory language is ambiguous and argued that if pricing affects access, the reasonable terms clause can include reasonable pricing. According to this view, the US government and its taxpayers, the largest public contributor to global scientific research and development, should not be paying the world's highest prices for drugs that it helped develop.

Discussion

Since 1980, the NIH has publicly reviewed 5 petitions requesting exercise of march-in rights related to 4 different health-related technologies or medicines developed from federal funding. In each of these circumstances, the NIH rejected the requests. Thus, since it was enacted 35 years ago, the march-in rights provision has remained unused, despite billions of dollars of government-sponsored research and the development of scores of transformative products emerging from such investments over this time.

March-in rights petitions continue to be filed by policymakers and invoked by advocates, most commonly in the context of high-cost new products developed from government-funded research. In reviewing the

details of past march-in rights cases and the opinions of our interviewees, we found what appears to be a solid legal basis for considering the excessively high price of a product to be a valid reason to invoke march-in rights. The legislative history of the Bayh-Dole Act and the plain language of the statute establish that the “reasonable terms” should take price into account, particularly if it is blatantly unreasonable and a key factor in limiting access to the product.⁴⁰

We also found convincing arguments from our interviewees about a regulatory and political climate offering little prospect that march-in rights would be invoked to regulate pricing of a health care product developed from federal funding. Several of the previous march-in rights petitions have outlined the detrimental effects of high prices on both US consumers and the economy. Yet march-in rights were not invoked in these cases, and it is difficult to envision more compelling scenarios, outside a price so exorbitant that a majority of patients and payers could simply not afford it (a still hypothetical situation). Furthermore, there is wide agreement on the NIH’s hesitancy to intervene: the NIH is both ill equipped to invoke a march-in petition and wary of the potentially negative ramifications that the enactment of march-in rights under Bayh-Dole could have on future commercialization.

It is worth noting that march-in rights are not the only mechanism available to public health advocates seeking to improve access or reduce high prices related to medical products arising from federally funded research. Another option might be to promote transparency in price-setting. For example, recently proposed legislation in California would require manufacturers to publicly disclose their drug development costs, which could provide greater accountability and justification for pricing.⁴¹ Still another option—though similarly unlikely to lead to the initiation of march-in rights in the current political climate—would be for the United States to establish an agency modeled after the United Kingdom’s National Institute for Health and Care Excellence (NICE) that could guide “fair” pricing through cost-effectiveness analysis.

As once suggested by Senator Ron Wyden (D-Ore.),⁴² the NIH could establish “payback” terms for drugs or technologies developed with federally funded patents.³⁹ Licenses for federally funded developments between universities and commercial entities would contain royalty terms. The company would then take the development through clinical trials and FDA approval, and if the product were profitable, it would pay a small royalty to the government to allow investment in further research.

The director of the NIH, Francis Collins, has endorsed this model as an acceptable alternative to an NIH-imposed oversight of prices.⁴³ Not only would this model allow companies to maintain pricing flexibility, but it also would provide the NIH with funding for future research.

Of course, even without the realistic prospect of invoking march-in rights, the US government maintains the power to claim access to any patented product, regardless of its funding sources, by issuing a compulsory license, in exchange for reasonable compensation.⁴⁴ This process, which in the past has provided access to items needed for warfare that infringe on patents, can be implemented directly by executive branch agencies without congressional approval, circumventing the bureaucratic steps of the march-in rights proceedings. The last time such a measure was invoked in the context of health care products was in 2001 during the anthrax scare, when the government was seeking to stockpile the antibiotic ciprofloxacin (Cipro) and Bayer demanded a high price. Faced with the threat of a compulsory license, Bayer reduced its price by 50%.^{45,46}

Conclusion

As the US government continues to invest in basic scientific research that will ultimately lead to commercially successful medical products, debates persist over access to and the costs of such products. Can the government's march-in rights under the Bayh-Dole Act help address these concerns? Our review suggests that the answer is generally no. At least under the current regulatory structure, the NIH will not intervene in the marketing of products that it or its grantees have helped discover, and march-in rights are not a viable strategy to address the cost of health care products developed from public funding. Based on experience to date, march-in rights may be useful only for cases in which a government-sponsored technology is licensed and then intentionally undeveloped, or for help in extracting minor concessions from licensees in extreme circumstances.

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Address correspondence to: Aaron S. Kesselheim, Program On Regulation, Therapeutics, And Law, Division of Pharmacoepidemiology and Pharmacoeconomics, 1620 Tremont St, Ste 3030, Boston, MA 02120 (email: akesselheim@partners.org).